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(FILE 'REGISTRY' ENTERED AT 11:27:20 ON 10 JAN 2003)
L1 277 SEA FILE=REGISTRY ABB=ON PLU=ON CC..P.C[7.]C|GCCSLPPCAL NNPDYC/SQSP
L9 87 SEA FILE=REGISTRY ABB=ON PLU=ON L1 AND SQL=<17

FILE 'HCAPLUS' ENTERED AT 11:25:31 ON 10 JAN 2003
L1 277 SEA FILE=REGISTRY ABB=ON PLU=ON CC..P.C[7.]C|GCCSLPPCAL NNPDYC/SQSP
L9 87 SEA FILE=REGISTRY ABB=ON PLU=ON L1 AND SQL=<17
L10 54 SEA FILE=HCAPLUS ABB=ON PLU=ON L9
L12 45 SEA FILE=HCAPLUS ABB=ON PLU=ON L10(L)ALPHA CONOTOXIN

L12 ANSWER 1 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:777965 HCAPLUS
DOCUMENT NUMBER: 137:289027
TITLE: Alpha conotoxin peptides with analgesic properties
INVENTOR(S): Livett, Bruce; Khalil, Zeinab; Gayler, Kenwyn; Down, John
PATENT ASSIGNEE(S): Australia
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002079236 | A1 | 20021010 | WO 2002-AU411 | 20020328 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AU 2001-4094 A 20010329
OTHER SOURCE(S): MARPAT 137:289027

AB This invention relates to novel .alpha.-conotoxin-like peptides comprising the following sequence of amino acids: Xaa1CCSXaa2Xaa3Xaa4CXaa5Xaa6Xaa7Xaa8Xaa9Xaa10Xaa11C-NH2 in which Xaa1 is G or D; Xaa3 is proline, hydroxyproline or glutamine; each of Xaa2 to Xaa8 and Xaa11 is independently any amino acid; Xaa9 is proline, hydroxyproline or glutamine; Xaa10 is aspartate, glutamate or .gamma.-carboxyglutamate; Xaa11 is optionally absent; and the C-terminus is optionally amidated, with the proviso that the peptide is not .alpha.-conotoxin Ep1 or .alpha.-conotoxin Im1. The peptides are useful in the treatment or prevention of pain, in recovery from nerve injury, and in the treatment of painful neurol. conditions such as stroke.

IT **467428-30-4 467428-33-7**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological

study); USES (Uses)
(**.alpha.-conotoxin** peptides with analgesic properties)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:520404 HCAPLUS
DOCUMENT NUMBER: 137:226853
TITLE: Methyllycaconitine is a potent antagonist of .alpha.-conotoxin-MII-sensitive presynaptic nicotinic acetylcholine receptors in rat striatum
AUTHOR(S): Mogg, Adrian J.; Whiteaker, Paul; McIntosh, J. Michael; Marks, Michael; Collins, Allan C.; Wonnacott, Susan
CORPORATE SOURCE: Department of Biology and Biochemistry, University of Bath, Bath, UK
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2002), 302(1), 197-204
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The plant alkaloid methyllycaconitine (MLA) is considered to be a selective antagonist of the .alpha.7 subtype of neuronal nicotinic acetylcholine receptor (nAChR). However, 50 nM MLA partially inhibited (by 16%) [3H]dopamine release from rat striatal synaptosomes stimulated with 10 .mu.M nicotine. Other .alpha.7-selective antagonists had no effect. Similarly, MLA (50 nM) inhibited [3H]dopamine release evoked by the partial agonist (2-chloro-5-pyridyl)-9-azabicyclo[4.2.1]non-2-ene (UB-165) (0.2 .mu.M) by 37%. In both cases, inhibition by MLA was surmountable with higher agonist concns., indicative of a competitive interaction. At least two subtypes of presynaptic nAChR can modulate dopamine release in the striatum, and these nAChR are distinguished by their differential sensitivity to .alpha.-conotoxin-MII (.alpha.-CTx-MII). MLA was not additive with a maximally effective concn. of .alpha.-CTx-MII (100 nM) in inhibiting [3H]dopamine release elicited by 10 .mu.M nicotine or 0.2 .mu.M UB-165, suggesting that both toxins act at the same site. This was confirmed in quant. binding assays with 125I-.alpha.-CTx-MII, which displayed saturable specific binding to rat striatum and nucleus accumbens with Bmax values of 9.8 and 16.5 fmol/mg of protein, and Kd values of 0.63 and 0.83 nM, resp. MLA fully inhibited 125I-.alpha.-CTx-MII binding to striatum and nucleus accumbens with a Ki value of 33 nM, consistent with the potency obsd. in the functional assays. The authors speculate that MLA and .alpha.-CTx-MII interact with a presynaptic nAChR of subunit compn. .alpha.3/.alpha.6.beta.2.beta.3* on dopamine neurons. The use of MLA as an .alpha.7-selective antagonist should be exercised with caution, esp. in studies of nAChR in basal ganglia.
IT **175735-93-0**, **.alpha.-Conotoxin**-MII
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(methyllycaconitine antagonism of **.alpha.**-

**conotoxin**-MII-sensitive presynaptic nicotinic receptors in dopamine release regulation in rat striatum)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:509427 HCAPLUS
TITLE: The synthesis and structure of an n-terminal dodecanoic acid conjugate of .alpha.-conotoxin MII
AUTHOR(S): Blanchfield, Joanne; Dutton, Julie; Hogg, Ron; Craik, David; Adams, David; Lewis, Richard; Alewood, Paul; Toth, Istvan
CORPORATE SOURCE: School of Pharmacy, The University of Queensland, Brisbane, Australia
SOURCE: Letters in Peptide Science (2002), Volume Date 2001, 8(3-5), 235-239
CODEN: LPSCEM; ISSN: 0929-5666
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The .alpha.-conotoxin MII is a 16 amino acid long peptide toxin isolated from the marine snail, Conus magus. This toxin has been found to be a highly selective and potent inhibitor of neuronal nicotinic acetylcholine receptors of the subtype .alpha.3.beta.2. To improve the bioavailability of this peptide, the authors have coupled 2-amino-DL-dodecanoic acid to the N-terminus of conotoxin MII creating a lipidic linear peptide, which was then successfully oxidized to produce the correctly folded conotoxin MII construct.
IT **186420-62-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of an aminododecanoic acid conjugate of **.alpha.-conotoxin** MII)
IT **175735-93-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of an aminododecanoic acid conjugate of **.alpha.-conotoxin** MII)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:458936 HCAPLUS
DOCUMENT NUMBER: 137:273401
TITLE: Differential nicotinic receptor expression in monkey basal ganglia: Effects of nigrostriatal damage
AUTHOR(S): Quik, M.; Polonskaya, Y.; McIntosh, J. M.; Kulak, J. M.
CORPORATE SOURCE: The Parkinson's Institute, Sunnyvale, CA, 94089, USA
SOURCE: Neuroscience (Oxford, United Kingdom) (2002), 112(3), 619-630
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors' previous work showed that there were marked declines in 125I-.alpha.-conotoxin MII labeled nicotinic receptors in monkey basal ganglia after nigrostriatal damage, findings that suggest .alpha.3/.alpha.6 contg. nicotinic receptors sites may be of relevance to Parkinson's disease. The authors now investigate whether there are differential changes in the distribution pattern of nicotinic receptor subtypes in the basal ganglia in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-lesioned animals compared to controls to better understand the changes occurring with nigrostriatal damage. To approach this the authors used 125I-.alpha.-conotoxin MII, a marker for .alpha.3/.alpha.6 nicotinic receptors, and 125I-epibatidine, a ligand that labels multiple nicotinic subtypes. The results demonstrate that there were medial to lateral gradients in nicotinic receptor distribution in control striatum, as well as ventromedial to dorsolateral gradients in the substantia nigra, which resembled those of the dopamine transporter in these same brain regions. Treatment with MPTP, a neurotoxin that selectively destroys dopaminergic nigrostriatal neurons, led to a relatively uniform decrease in nicotinic receptor sites in the striatum, but a differential effect in the substantia nigra with significantly greater declines in the ventrolateral portion. Competition anal. in the striatum showed that .alpha.-conotoxin MII sensitive sites were primarily affected after lesioning, whereas multiple nicotinic receptor populations were decreased in the substantia nigra. From these data the authors suggest that in the striatum .alpha.3/.alpha.6 nicotinic receptors are primarily localized on dopaminergic nerve terminals, while multiple nicotinic receptor subtypes are present on dopaminergic cell bodies in the substantia nigra. Thus, if activation of striatal nicotinic receptors is key in the regulation of basal ganglia function, .alpha.3/.alpha.6-directed nicotinic receptor ligands may be more relevant for Parkinson's disease therapy. However, nicotinic receptor ligands with a broader specificity may be more important if receptors in the substantia nigra play a dominant role in controlling nigrostriatal activity.

IT **175735-93-0, .alpha.-Conotoxin** MII
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(nicotinic receptor ligand; differential nicotinic receptor expression in monkey basal ganglia and effects of nigrostriatal damage)

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:449219 HCAPLUS
DOCUMENT NUMBER: 138:540
TITLE: Characterization of [125I]epibatidine binding and nicotinic agonist-mediated 86Rb+ efflux in interpeduncular nucleus and inferior colliculus of .beta.2 null mutant mice
AUTHOR(S): Marks, Michael J.; Whiteaker, Paul; Grady, Sharon R.; Picciotto, Marina R.; McIntosh, J. Michael; Collins, Allan C.
CORPORATE SOURCE: Institute for Behavioral Genetics, University of Colorado, Boulder, CO, 80309-0447, USA

SOURCE: Journal of Neurochemistry (2002), 81(5), 1102-1115
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The .beta.2 nicotinic acetylcholine receptor subunit null mutation eliminated most high affinity [3H]epibatidine binding in mouse brain, but significant binding remained in accessory olfactory nucleus, medial habenula, inferior colliculus and interpeduncular nucleus. Residual [125I]epibatidine binding sites in the inferior colliculus and interpeduncular nucleus were subsequently characterized. Inhibition of [125I]epibatidine binding by 12 agonists and six antagonists was very similar in these regions. Most acetylcholine-stimulated 86Rb+ efflux is eliminated in thalamus and superior colliculus of .beta.2 null mutants, but significant activity remained in inferior colliculus and interpeduncular nucleus. This residual activity was subsequently characterized. The 12 nicotinic agonists tested elicited concn.-dependent 86Rb+ efflux. Epibatidine was the most potent agonist. Cytisine was also potent and efficacious. EC50 values for quaternary agonists were relatively high. Cytisine-stimulated 86Rb+ efflux was inhibited by six classical nicotinic antagonists. Mecamylamine and D-tubocurarine were most potent, while decamethonium was the least potent. Agonists and antagonists exhibited similar potency in both brain regions. .alpha.-Bungarotoxin (100 nM) did not significantly inhibit cytisine-stimulated 86Rb+ efflux, while the .alpha.3.beta.4 selective antagonist, .alpha.ConotoxinAuIB, inhibited a significant fraction of the response in both brain regions. Thus, .beta.2 null mutant mice express residual nicotinic activity with properties resembling those of .alpha.3.beta.4*-nAChR.

IT **175735-93-0, .alpha.-Conotoxin** MII
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(characterization of [125I]epibatidine binding and nicotinic agonist-mediated 86Rb+ efflux in interpeduncular nucleus and inferior colliculus of .beta.2 null mutant mice)

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:324056 HCAPLUS
DOCUMENT NUMBER: 137:59609
TITLE: 5-Iodo-A-85380 binds to .alpha.-conotoxin MII-sensitive nicotinic acetylcholine receptors (nAChRs) as well as .alpha.4.beta.2* subtypes
AUTHOR(S): Kulak, Jennifer M.; Sum, Jocelyn; Musachio, John L.; McIntosh, J. Michael; Quik, Maryka
CORPORATE SOURCE: The Parkinson's Institute, Sunnyvale, CA, 94089-1605, USA
SOURCE: Journal of Neurochemistry (2002), 81(2), 403-406
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recent work suggests that 5-iodo-A-85380, a radioiodinated analog of the 3-pyridyl ether A-85380, represents a promising imaging agent

for non-invasive, in vivo studies of .alpha.4.beta.2* nicotinic acetylcholine receptors (nAChRs; *denotes receptors contg. the indicated subunits), because of its low non-specific binding, low in vivo toxicity and high selectivity for .alpha.4.beta.2* nAChRs. As an approach to elucidate nAChR subtypes expressed in striatum, we carried out competitive autoradiog. in monkey and rat brain using 5-[125I]iodo-A-85380 ([125I]A-85380) and [125I].alpha.-conotoxin MII, a ligand that binds with high affinity to .alpha.6* and .alpha.3* nAChRs, but not to .alpha.4.beta.2* nAChRs. Although A-85380 is reported to be selective for .alpha.4.beta.2* nAChRs, we obsd. that A-85380 completely inhibited [125I].alpha.-conotoxin MII binding in rat striatum and that A-85380 blocked >90% of [125I].alpha.-conotoxin MII sites in monkey caudate and putamen. These results suggest that A-85380 binds to non-.alpha.4.beta.2* nAChRs, including putative .alpha.6* nAChRs. Expts. to det. the percentage of [125I]A-85380 sites that contain .alpha.-conotoxin MII-sensitive (.alpha.6.beta.2*) nAChRs indicate that they represent about 10% of [125I]A-85380 sites in rodent striatum and about 30% of sites in monkey caudate and putamen. These data are important for identifying alterations in nicotinic receptor subtypes in Parkinson's disease and other basal ganglia disorders both in in vitro and in in vivo imaging studies.

IT **175735-93-0, .alpha.-Conotoxin** MII
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(5-iodo-A-85380 binds to **.alpha.-conotoxin** MII-sensitive nicotinic acetylcholine receptors)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:259386 HCAPLUS
DOCUMENT NUMBER: 136:396263
TITLE: Involvement of the .alpha.3 subunit in central nicotinic binding populations
AUTHOR(S): Whiteaker, Paul; Peterson, Cyrus G.; Xu, Wei; McIntosh, J. Michael; Paylor, Richard; Beaudet, Arthur L.; Collins, Allan C.; Marks, Michael J.
CORPORATE SOURCE: Inst. for Behavioral Genetics, Univ. of Colorado, Boulder, CO, 80309, USA
SOURCE: Journal of Neuroscience (2002), 22(7), 2522-2529
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The .alpha.3 subunit gene was one of the first neuronal nicotinic acetylcholine receptor (nAChR) subunits to be cloned (Boulter et al., 1986), but direct evidence of .alpha.3 subunit contributions to mammalian central nAChR populations has not been presented. The studies reported here used mice engineered to contain a null mutation in the .alpha.3 nAChR subunit gene (Xu et al., 1999) to examine the involvement of the .alpha.3 subunit in central nAChR populations. Heterologously expressed .alpha..beta..beta.2 and .alpha..beta..beta.4 nAChRs are pharmacol. similar to native [125I].alpha.-conotoxin MII (.alpha.-CtxMII)-binding and A 85380-resistant [125I]epibatidine-binding nAChR subtypes nAChRs was tested using quant. autoradiog. in .alpha.3-null mutant mice. Somewhat surprisingly, deletion of the .alpha.3 nAChR subunit gene

did not affect expression of the great majority of [125I].alpha.-CtxMII-binding sites, indicating that they do not correspond to heterologously expressed .alpha.3.beta.2 nAChRs. The only exception to this was obsd. in the habenulointerpeduncular tract, where .alpha.3-dependent [125I].alpha.-CtxMII binding was obsd. This finding may suggest the presence of an addnl., minor nicotinic population in this pathway. In contrast, most A 85380-resistant [125I]epibatidine-binding nAChRs were dependent on .alpha.3 gene expression, suggesting that they do indeed correspond to an .alpha.3 nAChR subtype. However, widespread but lower levels of .alpha.3-independent A 85380-resistant [125I]epibatidine binding were also seen. Again, this may indicate the existence of an addnl., minor population of non-.alpha.3 A 85380-resistant sites.

IT **175735-93-0, .alpha.-Conotoxin** MII
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nicotinic receptor characterization in brain of nicotinic receptor .alpha.3-subunit knockout mice)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:211177 HCAPLUS
DOCUMENT NUMBER: 137:76110
TITLE: A novel choline-sensitive nicotinic receptor subtype that mediates enhanced GABA release in the chick ventral lateral geniculate nucleus
AUTHOR(S): Guo, J.-Z.; Chiappinelli, V. A.
CORPORATE SOURCE: Department of Pharmacology, The George Washington University, School of Medicine and Health Sciences, Washington, DC, 20037, USA
SOURCE: Neuroscience (Oxford, United Kingdom) (2002), 110(3), 505-513
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We describe a novel choline-sensitive nicotinic receptor that mediates enhanced GABA release in the chick ventral lateral geniculate nucleus. Whole-cell recordings in slices demonstrated that choline (0.03-10 mM), generally considered an .alpha.7-selective agonist, and carbachol (3-300 .mu.M), a non-selective cholinergic agonist, both increased the frequency of spontaneous GABAergic events in ventral lateral geniculate nucleus neurons. Tetrodotoxin (0.5 .mu.M) partially reduced responses to carbachol, but eliminated responses to choline. During long-term (5 min) exposure to choline the GABA enhancement was maintained until choline was washed out. Choline (300 .mu.M) enhanced the frequency of spontaneous GABAergic events by 4.28-fold in control artificial cerebrospinal fluid. This choline-mediated enhancement was significantly reduced by the following nicotinic receptor antagonists: 1 .mu.M dihydro-.beta.-erythroidine (1.49-fold increase), 1 .mu.M methyllycaconitine (1.53-fold), and 0.2 .mu.M .alpha.-conotoxin ImI (1.84-fold). In contrast, no significant change was seen in the presence of 0.1 .mu.M dihydro-.beta.-erythroidine, 0.1 .mu.M methyllycaconitine, 0.1 .mu.M .alpha.-bungarotoxin, 0.1 .mu.M .alpha.-conotoxin MII, 0.1 .mu.M .kappa.-bungarotoxin, or 1 .mu.M .alpha.-conotoxin AuIB. These

results indicate that choline, at concns. as low as 100 .mu.M, activates a nicotinic receptor that is distinct from the classical 7 nicotinic receptors previously known to be activated by choline.

IT **175735-93-0, .alpha.-Conotoxin** MII
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(novel choline-sensitive nicotinic receptor subtype mediates GABA release in chick embryo ventral lateral geniculate nucleus)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:5325 HCAPLUS
DOCUMENT NUMBER: 136:65411
TITLE: Loss of nicotinic receptors in monkey striatum after 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine treatment is due to a decline in .alpha.-conotoxin MII sites
AUTHOR(S): Kulak, Jennifer M.; McIntosh, J. Michael; Quik, Maryka
CORPORATE SOURCE: The Parkinson's Institute, Sunnyvale, CA, USA
SOURCE: Molecular Pharmacology (2002), 61(1), 230-238
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nicotinic acetylcholine receptors (nAChRs) in the basal ganglia are a potential target for new therapeutics for Parkinson's disease. As an approach to detect expression of nAChRs in monkeys, we used 125I-epibatidine, an agonist at nAChRs contg. .alpha.2 to .alpha.6 subunits. 125I-Epibatidine binding sites are expressed throughout the control monkey brain, including the basal ganglia. The .alpha.3/.alpha.6-selective antagonist .alpha.-conotoxin MII maximally inhibited 50% of binding in the caudate-putamen and had no effect on 125I-epibatidine binding in the frontal cortex or thalamus. In contrast, inhibition expts. with nicotine, cytisine, and 3-(2(S)-azetidinylmethoxy)pyridine.cntdot.2HCl (A85380) showed a complete block of 125I-epibatidine binding in all regions investigated and did not discriminate between the .alpha.-conotoxin MII-sensitive and -insensitive populations in the striatum. To assess the effects of nigrostriatal damage, monkeys were rendered parkinsonian with the dopaminergic neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). Animals with moderate striatal damage (dopamine transporter levels .apprx.30% of control) had a 40 to 50% decrease in 125I-epibatidine binding. Inhibition studies showed that the decrease in epibatidine binding was due to loss of .alpha.-conotoxin MII-sensitive nAChRs. Monkeys with severe nigrostriatal damage (dopamine transporter levels .ltoreq.5% of control) exhibited a 55 to 60% decrease in 125I-epibatidine binding, which seemed to be due to a complete loss of .alpha.-conotoxin MII nAChRs and a partial loss of other nAChR subtypes. These results show that nAChRs expressed in the primate striatum have similar affinities for nicotine, cytisine, and A85380, that .alpha.-conotoxin MII discriminates between nAChR populations in the caudate and putamen, and that .alpha.-conotoxin MII-sensitive nAChRs are selectively decreased after MPTP-induced nigrostriatal damage.

IT **175735-93-0, .alpha.-Conotoxin** MII

RL: ADV (Adverse effect, including toxicity); ARG (Analytical reagent use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nicotinic receptors loss in monkey striatum after 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine treatment is due to a decline in **.alpha.-conotoxin** MII sites)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:549336 HCAPLUS
DOCUMENT NUMBER: 135:271222
TITLE: Vulnerability of 125I-.alpha.-conotoxin MII binding sites to nigrostriatal damage in monkey
AUTHOR(S): Quik, Maryka; Polonskaya, Yelena; Kulak, Jennifer M.; McIntosh, J. Michael
CORPORATE SOURCE: The Parkinson's Institute, Sunnyvale, CA, 94089, USA
SOURCE: Journal of Neuroscience (2001), 21(15), 5494-5500
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Parkinson's disease, a neurodegenerative movement disorder characterized by selective degeneration of nigrostriatal dopaminergic neurons, affects .apprx.1% of the population over 50. Because nicotinic acetylcholine receptors (nAChRs) may represent an important therapeutic target for this disorder, we performed expts. to elucidate the subtypes altered with nigrostriatal damage in parkinsonian monkeys. For this purpose we used 125I-.alpha.-conotoxin MII (CtxMII), a relatively new ligand that identifies .alpha.3 and/or .alpha.6 subunits contg. nAChR subtypes. In brain from untreated monkeys, there was saturable 125I-.alpha.-CtxMII binding to a single population of high-affinity nicotinic sites (Kd = 0.9 nM), primarily localized in the visual, habenula-interpeduncular, and nigrostriatal-mesolimbic pathways. Administration of the selective dopaminergic neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine resulted in damage to the nigrostriatal system and parkinsonism. Autoradiog. anal. showed that 125I-.alpha.-CtxMII sites were selectively reduced (.gtoreq.99%) in the basal ganglia and that the lesion-induced decreases correlated well with declines in the dopamine transporter, a marker of dopaminergic neuron integrity. These findings may indicate that most or all of 125I-.alpha.-CtxMII-labeled nAChR subtypes in the basal ganglia are present on nigrostriatal dopaminergic neurons, in contrast to 125I-epibatidine sites. These data suggest that the development of ligands directed to nAChR subtypes contg. .alpha.3 and/or .alpha.6 subunits may yield a novel treatment strategy for parkinsonian patients with nigrostriatal dopaminergic degeneration.

IT **175735-93-0, .alpha.-conotoxin** MII
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(vulnerability of 125I-**.alpha.-conotoxin** MII binding sites to nigrostriatal damage in monkey)

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:402212 HCAPLUS
DOCUMENT NUMBER: 135:134897
TITLE: An .alpha.4.beta.4 nicotinic receptor subtype is present in chick retina: identification, characterization and pharmacological comparison with the transfected .alpha.4.beta.4 and .alpha.6.beta.4 subtypes
AUTHOR(S): Barabino, Benedetta; Vailati, Silvia; Moretti, Milena; McIntosh, J. Michael; Longhi, Renato; Clementi, Francesco; Gotti, Cecilia
CORPORATE SOURCE: Department of Experimental Medicine and Pathology, La Sapienza University, Rome, Italy
SOURCE: Molecular Pharmacology (2001), 59(6), 1410-1417
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Retina from 1-day-old chicks is a valuable tissue model for studying neuronal nicotinic receptors because it expresses a large no. of the developmentally regulated high-affinity [3H]epibatidine labeled nicotinic receptors. Most of these receptors contain the .beta.4 subunit assocd. with different .alpha. subunits. Using a sequential immunodepletion procedure with anti-.alpha.6, anti-.beta.3, anti-.beta.2, and anti-.beta.4 antibodies, we purified an .alpha.4.beta.4 nicotinic receptor subtype that accounts for .apprx.20-25% of the high-affinity [3H]epibatidine labeled receptors present in retina at that developmental time. Immunopptn. and Western blotting expts. confirmed that the purified subtype contains only the .alpha.4 and .beta.4 subunits. This receptor binds a no. of agonists and the antagonist dihydro-.beta.-erythroidine with nanomolar affinity, whereas it has micromolar affinity for the .alpha.-conotoxin MII and methyllycaconitine toxins and other nicotinic antagonists. Comparison of the pharmacol. profile of this purified native subtype with that of the same subtype transiently expressed in human BOSC23 cells showed that they have very similar rank orders and abs. Ki values for several nicotinic drugs. Finally, because chick retina expresses an .alpha.6.beta.4-contg. subtype with a high affinity for the .alpha.-conotoxin MII, we used native and transfected .alpha.4.beta.4 and .alpha.6.beta.4 subtypes to investigate the relative contributions of the .alpha. and .beta. subunits to this binding, and found that the .alpha.6 subunit dets. the high affinity for this toxin.

IT **175735-93-0, .alpha.-conotoxin** MII
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(identification, characterization, and pharmacol. comparison of .alpha.4.beta.4 nicotinic receptor in chick retina)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:380120 HCAPLUS
DOCUMENT NUMBER: 135:137700
TITLE: An efficient synthetic scheme for natural .alpha.-conotoxins and their analogues
AUTHOR(S): Zhmak, M. N.; Kasheverov, I. E.; Utkin, Yu. N.; Tsetlin, V. I.; Vol'pina, O. M.; Ivanov, V. T.
CORPORATE SOURCE: Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, Moscow, 117997, Russia
SOURCE: Russian Journal of Bioorganic Chemistry (Translation of Bioorganicheskaya Khimiya) (2001), 27(2), 67-71
CODEN: RJBCET; ISSN: 1068-1620
PUBLISHER: MAIK Nauka/Interperiodica
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An efficient scheme for the synthesis of .alpha.-conotoxins, contg. 12-18 amino acid residues and two disulfide bridges, was proposed. Its advantages are: (1) the avoidance of orthogonal protections of Cys residues; (2) a lower no. of stages in a cycle of the peptide chain elongation by the method of solid phase synthesis; (3) the linear product is sufficiently pure for being used at the next stage of the disulfide bond formation without addnl. purifn.; and (4) a substantially reduced time of oxidn. to disulfides at pH 10, which led to the target product in a high yield. A no. of natural .alpha.-conotoxins (GI, ImI, EI, MII, and SIA), affecting the muscle and neuronal nicotinic acetylcholine receptors of various types, and several new analogs of these conotoxins (in particular, [Tyr10]ImI, [Gln12]GI, and [Ser1]GI) were synthesized by this scheme. They were used for elucidating the spatial structure of .alpha.-conotoxins by 1H NMR spectroscopy and for studying the ligand-binding sites of their receptors.
IT **175735-93-0P, .alpha.-Conotoxin** M II
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid phase synthesis of natural **alpha conotoxins** and their analogs)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:513711 HCAPLUS
DOCUMENT NUMBER: 133:131093
TITLE: Protein and cDNA sequences of Conus .alpha.-conotoxins and the therapeutic uses thereof as neuromuscular blocking agent
INVENTOR(S): Olivera, Baldomero M.; Layer, Richard T.; Watkins, Maren; Hillyard, David R.; McIntosh, J. Michael; Jones, Robert M.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA; Cognetix, Inc.
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000043409 | A2 | 20000727 | WO 2000-US1372 | 20000121 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2000027327 | A5 | 20000807 | AU 2000-27327 | 20000121 |
| US 6268473 | B1 | 20010731 | US 2000-488799 | 20000121 |
| EP 1159288 | A1 | 20011205 | EP 2000-905680 | 20000121 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |

PRIORITY APPLN. INFO.: US 1999-116881P P 19990122
US 1999-116882P P 19990122
WO 2000-US1372 W 20000121

OTHER SOURCE(S): MARPAT 133:131093

AB The invention provides protein and cDNA sequences of Conus .alpha.-conotoxins. Conus .alpha.-conotoxins are relatively short peptides, about 10-25 residues in length, and are naturally available in minute amts. in the venom of the cone snails. The invention further relates to the therapeutic uses of the Conus .alpha.-conotoxins as neuromuscular blocking agents, such as muscle relaxants for treating benign essential blepharospasm and other forms of focal dystonia and for anti-wrinkle use.

IT **285558-22-7P 285558-23-8P 285558-24-9P**
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(protein and cDNA sequences of Conus **.alpha.-conotoxins** and therapeutic uses thereof as neuromuscular blocking agent)

L12 ANSWER 14 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:303382 HCAPLUS
DOCUMENT NUMBER: 133:38562
TITLE: 125I-.alpha.-conotoxin MII identifies a novel nicotinic acetylcholine receptor population in mouse brain
AUTHOR(S): Whiteaker, Paul; Mcintosh, J. Michael; Luo, Siqin; Collins, Allan C.; Marks, Michael J.
CORPORATE SOURCE: Institute for Behavioral Genetics, University of Colorado, Boulder, CO, USA
SOURCE: Molecular Pharmacology (2000), 57(5), 913-925
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB .alpha.-Conotoxin MII (CtxMII), a peptide toxin from the venom of the predatory cone snail Conus magus, displays an unusual nicotinic pharmacol. Specific binding of a radioiodinated deriv. (125I-.alpha.-CtxMII) was identified in brain region homogenates and

tissue sections. Quant. autoradiog. indicated that 125I-.alpha.-CtxMII binding sites have an unique pharmacol. profile and distribution in mouse brain, being largely confined to the superficial layers of the superior colliculus, nigrostriatal pathway, optic tract, olivary pretectal, and mediolateral and dorsolateral geniculate nuclei. Expression of .alpha.-CtxMII binding sites in the nigrostriatal pathway, combined with evidence for .alpha.-CtxMII-sensitivity of nicotine-induced [3H]dopamine release in rodent striatal prepns. indicates that 125I-.alpha.-CtxMII binding nicotinic acetylcholine receptors are likely to be physiol. important. Unlabeled .alpha.-CtxMII potently (Ki <3 nM) competed for a subset of [3H]epibatidine binding sites in mouse brain homogenates, but weakly (IC50 >10 .mu.M) interacted with 125I-.alpha.-bungarotoxin and (-)-[3H]nicotine binding sites, confirming this compd.'s novel nicotinic pharmacol. Quant. autoradiog. revealed that .alpha.-CtxMII binds with high affinity at a subset of [3H]epibatidine binding sites with relatively low cytisine affinity ("cytisine-resistant" sites), resolving [3H]epibatidine binding into three different populations, each probably corresponding to a receptor subtype. The majority population seems to correspond to that which binds nicotine and cytisine with high affinity ("cytisine-sensitive" sites). Comparison of the cytisine-resistant population's distribution with that of .alpha.3 subunit mRNA expression suggests that the fractions both more and less sensitive to .alpha.-CtxMII probably contain the .alpha.3 subunit, perhaps in combination with different .beta. subunits.

IT **175735-93-0, .alpha.-Conotoxin** MII
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**.alpha.-conotoxin** MII-binding nicotinic acetylcholine receptor population in mouse brain and distribution and function and pharmacol. characterization thereof)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 15 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:256009 HCAPLUS
DOCUMENT NUMBER: 133:13021
TITLE: Conus peptides: novel probes for nicotinic acetylcholine receptor structure and function
AUTHOR(S): McIntosh, J. M.; Gardner, S.; Luo, S.; Garrett, J. E.; Yoshikami, D.
CORPORATE SOURCE: Department of Psychiatry, University of Utah, Salt Lake City, UT, USA
SOURCE: European Journal of Pharmacology (2000), 393(1-3), 205-208
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Conus is a genus of predatory marine snails that uses venom to capture prey. Among the neurotoxins widely utilized by the cone snails are the .alpha.-conotoxins which are disulfide-rich peptides that target muscle or neuronal subtypes of nicotinic acetylcholine receptors. The small size and receptor subtype specificity of these

peptides make them particularly useful for characterizing both native and heterologously expressed nicotinic receptors. In this report, we demonstrate that .alpha.-conotoxin MII potently blocks .beta.3-contg. neuronal nicotinic receptors. Furthermore, initial evidence suggests that subpopulations of .alpha.3.beta.2.beta.3-contg. receptors are differentially sensitive to .alpha.-conotoxin MII. Thus, .alpha.-conotoxin MII promises to be a useful tool for studying neuronal nicotinic receptors contg. the .beta.3 subunit.

IT **175735-93-0, .alpha.-Conotoxin** MII
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Conus peptides as probes for nicotinic acetylcholine receptor structure and function)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 16 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:255989 HCAPLUS
DOCUMENT NUMBER: 133:14832
TITLE: .beta.3 Subunit is present in different nicotinic receptor subtypes in chick retina
AUTHOR(S): Vailati, S.; Moretti, M.; Balestra, B.; McIntosh, M.; Clementi, F.; Gotti, C.
CORPORATE SOURCE: University of Milan, Department of Medical Pharmacology, CNR Cellular and Molecular Pharmacology Center, Milan, 20129, Italy
SOURCE: European Journal of Pharmacology (2000), 393(1-3), 23-30
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using subunit-specific antibodies and immunopptn. expts., we have identified the retina as being the chick central nervous system (CNS) area that expresses the highest level of the .beta.3 subunit. Sequential immunopurifn. expts. showed that there are .gtoreq.2 populations of .beta.3-contg. receptors in chick retina: in one, the .beta.3 subunit is assocd. with the .alpha.6 and .beta.4 subunits; in the other more heterogeneous population, the .beta.3 subunit is assocd. with the .alpha.2, .alpha.3, .alpha.4, .beta.2, and .beta.4 subunits. Both of these receptor populations bind [3H]epibatidine and a no. of nicotinic receptor agonists with high affinity (nM) and nicotinic receptor antagonists with a lower affinity (.mu.M). The greatest pharmacol. difference between the 2 populations is the affinity for the .alpha.-conotoxin MII, which inhibits binding to .alpha.6-contg. receptors and not that to .beta.3-contg. receptors. We also searched for the presence of the .beta.3 subunit assocd. with the .alpha.-bungarotoxin binding subunits .alpha.7 and/or .alpha.8 in retina and chick brain. Immunopptn. studies using anti-.beta.3 antibodies did not detect any specific .alpha.-bungarotoxin labeled receptors, thus, indicating that the .beta.3 subunit is not present in the .alpha.-bungarotoxin receptors of these areas.

IT **175735-93-0, .alpha.-Conotoxin** M II
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(.beta.3 subunit is present in different nicotinic receptor subtypes in chick retina)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 17 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:243855 HCAPLUS

DOCUMENT NUMBER: 132:343676

TITLE: UB-165: A novel nicotinic agonist with subtype selectivity implicates the .alpha.4.beta.2* subtype in the modulation of dopamine release from rat striatal synaptosomes

AUTHOR(S): Sharples, Christopher G. V.; Kaiser, Sergio; Soliakov, Lev; Marks, Michael J.; Collins, Allan C.; Washburn, Mark; Wright, Emma; Spencer, James A.; Gallagher, Timothy; Whiteaker, Paul; Wonnacott, Susan

CORPORATE SOURCE: Department of Biology and Biochemistry, University of Bath, Bath, BA2 7AY, UK

SOURCE: Journal of Neuroscience (2000), 20(8), 2783-2791
CODEN: JNRSDS; ISSN: 0270-6474

PUBLISHER: Society for Neuroscience

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Presynaptic nicotinic acetylcholine receptors (nAChRs) on striatal synaptosomes stimulate dopamine release. Partial inhibition by the .alpha.3.beta.2-selective .alpha.-conotoxin-MII indicates heterogeneity of presynaptic nAChRs on dopamine terminals. We have used this .alpha.-conotoxin and UB-165, a novel hybrid of epibatidine and anatoxin-1, to address the hypothesis that the .alpha.-conotoxin-MII-insensitive subtype is composed of .alpha.4 and .beta.2 subunits. UB-165 shows intermediate potency, compared with the parent mols., at .alpha.4.beta.2* and .alpha.3-contg. binding sites, and resembles epibatidine in its high discrimination of these sites over .alpha.7-type and muscle binding sites. (.+-.)-Epibatidine, (.+-.)-anatoxin-a, and (.+-.)-UB-165 stimulated [3H]-dopamine release from striatal synaptosomes with EC50 values of 2.4, 134, and 88 nM, and relative efficacies of 1:0.4:0.2, resp. .alpha.-Conotoxin-MII inhibited release evoked by these agonists by 48, 56, and 88%, resp., suggesting that (.+-.)-UB-165 is a very poor agonist at the .alpha.-conotoxin-MII-insensitive nAChR subtype. In assays of 86Rb+ efflux from thalamic synaptosomes, a model of an .alpha.4.beta.2* nAChR response, (.+-.)-UB-165 was a very weak partial agonist; the low efficacy of (.+-.)-UB-165 at .alpha.4.beta.2 nAChR was confirmed in Xenopus oocytes expressing various combinations of human nAChR subunits. In contrast, (.+-.)-UB-165 and (.+-.)-anatoxin-a were similarly efficacious and similarly sensitive to .alpha.-conotoxin-MII in increasing intracellular Ca2+ in SH-SY5Y cells, a functional assay for native .alpha.3-contg. nAChR. These data support the involvement of .alpha.4.beta.2* nAChR in the presynaptic modulation of striatal dopamine release and illustrate the utility of exploiting a novel partial agonist, together with a selective antagonist, to dissect the functional roles of nAChR subtypes in the brain.

IT **175735-93-0, .alpha.-Conotoxin-MII**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(UB-165 nicotinic agonist subtype selectivity implicates .alpha.4.beta.2* subtype in modulation of dopamine release from rat striatal synaptosomes)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 18 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:191100 HCAPLUS
DOCUMENT NUMBER: 132:237373
TITLE: Preparation of cyclized conotoxin peptides
INVENTOR(S): Craik, David James; Daly, Norelle Lee; Nielsen, Katherine Justine
PATENT ASSIGNEE(S): University of Queensland, Australia
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000015654 | A1 | 20000323 | WO 1999-AU769 | 19990914 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9960705 | A1 | 20000403 | AU 1999-60705 | 19990914 |
| AU 747006 | B2 | 20020509 | | |
| EP 1129106 | A1 | 20010905 | EP 1999-947111 | 19990914 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |

PRIORITY APPLN. INFO.: AU 1998-5895 A 19980914
WO 1999-AU769 W 19990914

AB Cyclized conotoxin peptides were prepd. for the therapeutic treatment of mammals. Thus, cyclo[CKGKGAKCSRLMYDCCTGSCRSGKCTRNGLPG] , a cyclic analog of MVIIA having the linking moiety TRNGLPG, was prepd. by the solid-phase method.

IT **175735-93-0DP, .alpha.-Conotoxin** M II, cyclic analogs **195823-99-5DP, .alpha.-Conotoxin** Pn IB, cyclic analogs **195824-00-1DP, .alpha.-Conotoxin** Pn IA, cyclic analogs
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyclized conotoxin peptides)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 19 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:156025 HCAPLUS
DOCUMENT NUMBER: 132:318808

TITLE: Leu10 of .alpha.-conotoxin PnIB confers potency for neuronal nicotinic responses in bovine chromaffin cells

AUTHOR(S): Broxton, N.; Miranda, L.; Gehrmann, J.; Down, J.; Alewood, P.; Livett, B.

CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, University of Melbourne, Parkville, Australia

SOURCE: European Journal of Pharmacology (2000), 390(3), 229-236
CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two .alpha.-conotoxins PnIA and PnIB (previously reported as being "mollusk specific") which differ in only two amino acid residues (AN vs. LS at residues 10 and 11, resp.), show markedly different inhibition of the neuronal nicotinic acetylcholine receptor response in bovine chromaffin cells, a mammalian prepn. Whereas .alpha.-conotoxin PnIB completely inhibits the nicotine-evoked catecholamine release at 10 .mu.M, with IC50 = 0.7 .mu.M, .alpha.-conotoxin PnIA is some 30-40 times less potent. Two peptide analogs, [A10L]PnIA and [N11S]PnIA were synthesized to investigate the extent to which each residue contributes to activity. [A10L]PnIA (IC50 = 2.0 .mu.M) completely inhibits catecholamine release at 10 .mu.M, whereas [N11S]PnIA shows little inhibition. In contrast, none of the peptides inhibit muscle-type nicotinic responses in the rat hemi-diaphragm prepn. The authors conclude that the enhanced potency of .alpha.-conotoxin PnIB over .alpha.-conotoxin PnIA in the neuronal-type nicotinic response is principally detd. by the larger, more hydrophobic leucine residue at position 10 in .alpha.-conotoxin PnIB.

IT **195823-99-5**, **.alpha.-Conotoxin** PnIB
**195824-00-1**, **.alpha.-Conotoxin** PnIA
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(Leu10 of **.alpha.-conotoxin** PnIB confers potency for neuronal nicotinic responses in bovine chromaffin cells)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 20 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:148514 HCAPLUS

DOCUMENT NUMBER: 132:246458

TITLE: Pairwise interactions between neuronal .alpha.7 acetylcholine receptors and .alpha.-conotoxin PnIB

AUTHOR(S): Quiram, P. A.; McIntosh, J. M.; Sine, S. M.

CORPORATE SOURCE: Receptor Biology Laboratory, Department of Physiology and Biophysics Mayo Foundation, Rochester, MN, 55905, USA

SOURCE: Journal of Biological Chemistry (2000), 275(7), 4889-4896
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal
LANGUAGE: English

AB This work uses .alpha.-conotoxin PnIB to probe the agonist binding site of neuronal .alpha.7 acetylcholine receptors. We mutated the 13 non-cysteine residues in CTx PnIB, expressed .alpha.7/5-hydroxytryptamine-3 homomeric receptors in 293 HEK cells, and measured binding of each mutant toxin to the expressed receptors by competition against the initial rate of 125I-.alpha.-bungarotoxin binding. The results reveal that residues Ser-4, Leu-5, Pro-6, Pro-7, Ala-9, and Leu-10 endow CTx PnIB with affinity for .alpha.7/5-hydroxytryptamine-3 receptors; side chains of these residues cluster in a localized region within the three-dimensional structure of CTx PnIB. We next mutated key residues in the seven loops of .alpha.7 that converge at subunit interfaces to form the agonist binding site. The results reveal predominant contributions by residues Trp-149 and Tyr-93 in .alpha.7 and smaller contributions by Ser-34, Arg-186, Tyr-188, and Tyr-195. To identify pairwise interactions that stabilize the receptor-conotoxin complex, we measured binding of receptor and toxin mutations and analyzed the results by double mutant cycles. The results reveal a single dominant interaction between Leu-10 of CTx PnIB and Trp-149 of .alpha.7 that anchors the toxin to the binding site. We also find weaker interactions between Pro-6 of CTx PnIB and Trp-149 and between both Pro-6 and Pro-7 and Tyr-93 of .alpha.7. The overall results demonstrate that a localized hydrophobic region in CTx PnIB interacts with conserved arom. residues on one of the two faces of the .alpha.7 binding site.

IT **195823-99-5, .alpha.-Conotoxin** Pn IB
**195824-00-1, .alpha.-Conotoxin** Pn IA
**221639-83-4 229639-63-8 263028-53-1**
**263028-54-2 263028-55-3 263028-56-4**
**263028-57-5 263028-58-6 263028-59-7**
**263028-61-1 263028-62-2 263028-63-3**
**263028-64-4 263028-65-5 263028-66-6**
**263028-67-7 263028-68-8 263028-69-9**
**263028-70-2 263028-71-3 263028-72-4**
**263028-73-5 263028-74-6 263028-75-7**
**263028-76-8 263028-77-9 263028-78-0**
**263028-79-1 263028-80-4 263028-81-5**
**263028-82-6 263028-83-7 263028-84-8**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(neuronal .alpha.7 acetylcholine receptor and **.alpha.-conotoxin** PnIB pairwise interactions and structure-activity relations therein)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 21 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:2224 HCAPLUS
DOCUMENT NUMBER: 132:132466
TITLE: Single amino acid substitutions in .alpha.-conotoxin PnIA shift selectivity for subtypes of the mammalian neuronal nicotinic acetylcholine receptor
AUTHOR(S): Hogg, Ron C.; Miranda, Les P.; Craik, David J.; Lewis, Richard J.; Alewood, Paul F.; Adams,

David J.
CORPORATE SOURCE: The Department of Physiology and Pharmacology, University of Queensland, Brisbane, 4072, Australia
SOURCE: Journal of Biological Chemistry (1999), 274(51), 36559-36564
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The .alpha.-conotoxins, a class of nicotinic acetylcholine receptor (nAChR) antagonists, are emerging as important probes of the role played by different nAChR subtypes in cell function and communication. In this study, the native .alpha.-conotoxins PnIA and PnIB were found to cause concn.-dependent inhibition of the ACh-induced current in all rat parasympathetic neurons examd., with IC50 values of 14 and 33 nM, and a maximal redn. in current amplitude of 87% and 71%, resp. The modified .alpha.-conotoxin [N11S]PnIA reduced the ACh-induced current with an IC50 value of 375 nM and a maximally effective concn. caused 91% block. [A10L]PnIA was the most potent inhibitor, reducing the ACh-induced current in .apprx.80% of neurons, with an IC50 value of 1.4 nM and 46% maximal block of the total current. The residual current was not inhibited further by .alpha.-bungarotoxin, but was further reduced by the .alpha.-conotoxins PnIA or PnIB, and by mecamylamine. 1H NMR studies indicate that PnIA, PnIB, and the analogs, [A10L]PnIA and [N11S]PnIA, have identical backbone structures. The authors propose that positions 10 and 11 of PnIA and PnIB influence potency and det. selectivity among .alpha.7 and other nAChR subtypes, including .alpha.3.beta.2 and .alpha.3.beta.4. Four distinct components of the nicotinic ACh-induced current in mammalian parasympathetic neurons have been dissected with these conopeptides.
IT **195824-00-1, .alpha.-Conotoxin** PnIA
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid substitutions in **.alpha.-conotoxin** PnIA shift selectivity for subtypes of mammalian neuronal nicotinic acetylcholine receptor)
IT **195823-99-5, .alpha.-Conotoxin** PnIB
**221639-83-4 229639-63-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(single amino acid substitutions in **.alpha.-conotoxin** PnIA shift selectivity for subtypes of mammalian neuronal nicotinic acetylcholine receptor)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 22 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:649491 HCAPLUS
DOCUMENT NUMBER: 132:9825
TITLE: Single-Residue Alteration in .alpha.-Conotoxin

PnIA Switches Its nAChR Subtype Selectivity
AUTHOR(S): Luo, S.; Nguyen, T. A.; Cartier, G. E.; Olivera, B. M.; Yoshikami, D.; McIntosh, J. M.
CORPORATE SOURCE: Department of Biology, University of Utah, Salt Lake City, UT, 84112, USA
SOURCE: Biochemistry (1999), 38(44), 14542-14548
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB .alpha.-Conotoxins are disulfide-rich peptides that are competitive antagonists of nicotinic acetylcholine receptors (nAChRs). Despite their small size, different .alpha.-conotoxins are able to discriminate among different subtypes of mammalian nAChRs. In this report, the activity of two peptides from the venom of Conus pennaceus, .alpha.-conotoxins PnIA and PnIB, are examd. Although the toxins differ in only two residues, PnIA preferentially blocks .alpha.3.beta.2 nAChRs, whereas PnIB prefers the .alpha.7 subtype. Point mutation chimeras of these .alpha.-conotoxins were synthesized and their activities assessed on Xenopus oocytes expressing specific nAChRs. Change of a single residue, Ala10 to Leu, in PnIA (to form PnIA [A10L]) converts the parent peptide from .alpha.3.beta.2-preferring to .alpha.7-preferring; furthermore, PnIA [A10L] blocks the .alpha.7 receptor with an IC50 (12.6 nM) that is lower than that of either parent peptide. Kinetic anal. indicates that differences in affinity among the analogs are primarily due to differences in off-rate, with PnIA [A10L]'s interaction with .alpha.7 having the smallest off-rate (koff = 0.17 min-1). Thermodn. anal. indicates that Leu10 enhances the peptide's interaction with .alpha.7, but not .alpha.3.beta.2, receptors, whereas Ser11 (in PnIA [N11S]) reduces its affinity for both .alpha.7 and .alpha.3.beta.2 nAChRs.

IT **195824-00-1**, **.alpha.-Conotoxin** PnIA
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(single-residue alteration in **.alpha.-conotoxin** PnIA switches nAChR subtype selectivity)

IT **195823-99-5**, **.alpha.-Conotoxin** PnIB
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(single-residue alteration in **.alpha.-conotoxin** PnIA switches nAChR subtype selectivity in relation to PnIB)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 23 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:468432 HCAPLUS
DOCUMENT NUMBER: 131:82983
TITLE: Uses of alpha-conotoxin peptides
INVENTOR(S): Olivera, Baldomero M.; Mcintosh, J. Michael; Yoshikami, Doju; Cartier, G. Edward; Luo, Siqin
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9933482 | A1 | 19990708 | WO 1998-US27367 | 19981223 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9920917 | A1 | 19990719 | AU 1999-20917 | 19981223 |
| US 6265541 | B1 | 20010724 | US 1998-219446 | 19981223 |
| US 2002022715 | A1 | 20020221 | US 2001-897465 | 20010703 |

PRIORITY APPLN. INFO.:

| | | | |
|---|---|---|---|
| US 1997-70153P | P | 19971231 |
| US 1998-80588P | P | 19980403 |
| US 1998-219446 | A3 | 19981223 |
| WO 1998-US27367 | W | 19981223 |

OTHER SOURCE(S): MARPAT 131:82983

AB The present invention relates to the use of .alpha.-conotoxin peptides having the general formula: Xaa1-Xaa2-Cys-Cys-Xaa3-Xaa4-Pro-Xaa5-Cys-Xaa6-Cys (SEQ ID NO.1) for treating disorders regulated at neuronal nicotinic acetylcholine receptors. Such disorders include, but are not limited to, cardiovascular disorders, gastric motility disorders, urinary incontinence, nicotine addiction, mood disorders (such as bipolar disorder, unipolar depression, dysthymia and seasonal effective disorder) and small cell lung carcinoma, as well as the localization of small cell lung carcinoma. In this formula, Xaa1 is des-Xaa1, Tyr, mono-iodo-Tyr or di-iodo-Tyr, Xaa2 is any amino acid, Xaa3 is any amino acid, Xaa4 is any amino acid, Xaa5 is any amino acid and Xaa6 represents a peptide of 3-7 amino acids. Disulfide linkages exist between the first and third cysteines and the second and fourth cysteines. Pro may be replaced with hydroxy-Pro. The C-terminus may contain a hydroxyl or an amide group, preferably an amide group.

IT **216299-20-6P**, **.alpha.-Conotoxin** AuIA
**221639-83-4P** **223416-43-1P**, **.alpha.-Conotoxin** AuIC **229639-60-5P** **229639-61-6P**
**229639-63-8P** **229639-64-9DP**, radiolabeled
**229639-64-9P** **229639-65-0DP**, radiolabeled
**229639-65-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(uses of **alpha-conotoxin** peptides as nicotinic antagonists in relation to treatment neuronal nicotinic receptor disorders effect on neurotransmitter release)

IT **175735-93-0**, **.alpha.-Conotoxin** MII
**195823-99-5**, **.alpha.-Conotoxin** PnIB
**195824-00-1**, **.alpha.-Conotoxin** PnIA
**229639-62-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(uses of **alpha-conotoxin** peptides as

nicotinic antagonists in relation to treatment neuronal nicotinic receptor disorders effect on neurotransmitter release)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 24 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:457542 HCAPLUS
DOCUMENT NUMBER: 131:211802
TITLE: Functional .alpha.6-containing nicotinic receptors are present in chick retina
AUTHOR(S): Vailati, Silvia; Hanke, Wolfgang; Bejan, Andreea; Barabino, Benedetta; Longhi, Renato; Balestra, Barbara; Moretti, Milena; Clementi, Francesco; Gotti, Cecilia
CORPORATE SOURCE: Consiglio Nazionale delle Ricerche (CNR) Cellular and Molecular Pharmacology Center, Department of Medical Pharmacology, University of Milan, Milan, Italy
SOURCE: Molecular Pharmacology (1999), 56(1), 11-19 CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Despite the fact that the neuronal chick .alpha.6 subunit was first cloned several years ago and recently has been shown to form acetylcholine (ACh)-activated channels in heterologous systems, no information is yet available concerning the structure and function of the .alpha.6-contg. nicotinic receptors in neuronal tissues. Using subunit-specific antibodies directed against 2 different epitopes of the chick .alpha.6 subunit, we performed immunopptn. expts. on immunopurified .alpha.6-contg. receptors radiolabeled with the nicotinic agonist [3H]epibatidine (Epi): almost all of the .alpha.6 receptors contained the .beta.4 subunit, 51% the .beta.3 subunit, 42% the .alpha.3 subunit, and 7.5% the .beta.2 subunit. Western blot analyses of the purified receptors confirmed the presence of the .alpha.3, .beta.3, .beta.2, and .beta.4 subunits, and the absence of the .alpha.4, .alpha.5, and .alpha.7 subunits. The .alpha.6-contg. receptors bind [3H]Epi (Kd = 35 pM) and a no. of other nicotinic agonists with very high affinity, the rank order being Epi >> cytisine > nicotine > 1,1-dimethyl-4-phenylpiperazinium > acetylcholine > carbamylcholine. The .alpha.6 receptors also have a distinct antagonist pharmacol. profile with a rank order of potency of .alpha.-conotoxin MII > methyllycaconitine > dihydro-.beta.-erythroidine > MG624 > d-tubocurarine > decamethonium > hexamethonium. When reconstituted in lipid bilayers, the .alpha.6-contg. receptors form functional cationic channels with a main conductance state of 48 pS. These channels are activated by nicotinic agonists in a dose-dependent manner, and blocked by the nicotinic antagonist d-tubocurarine.
IT **175735-93-0, .alpha.-Conotoxin** MII
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(functional .alpha.6-contg. nicotinic receptors are present in chick retina)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE

IN THE RE FORMAT

L12 ANSWER 25 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:334877 HCAPLUS
DOCUMENT NUMBER: 131:84191
TITLE: Inhibition of nicotine-induced hippocampal norepinephrine release in rats by alpha-conotoxins MII and AuIB microinjected into the locus ceruleus
AUTHOR(S): Fu, Yitong; Matta, Shannon G.; McIntosh, J. Michael; Sharp, Burt M.
CORPORATE SOURCE: Department of Pharmacology, University of Tennessee-Memphis, Memphis, TN, 38163, USA
SOURCE: Neuroscience Letters (1999), 266(2), 113-116
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hippocampal norepinephrine (NE) is secreted by neurons projecting from the locus ceruleus (LC) to the hippocampus; LC nicotinic receptors (NAchRs) are involved in the effects of systemic nicotine on this pathway. To clarify the NAchR subtypes, NAchR antagonists, termed a-conotoxins, were microinjected into the LC before nicotine; MII and AuIB were used to assess the potential involvement of .alpha.3.beta.2 and .alpha.3.beta.4 subunit-contg. NAchRs, resp. Nicotine dose-dependently stimulated hippocampal NE release ($P < 0.01$); MII (>0.25 pmol) reduced the NE response to nicotine (67% decrease; $P < 0.05$), as did AuIB (44% redn. by 25 pmol; $P < 0.05$). Administered together, however, MII and AuIB were no more effective than MII. Thus, MII and AuIB are capable of interacting with NAchR subtypes other than those previously defined as .alpha.3.beta.2 and .alpha.3.beta.4, resp. NAchRs contg. both .beta.2 and .beta.4 subunits may be involved.
IT **175735-93-0, .alpha.-Conotoxin** MII
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(inhibition of nicotine-induced hippocampal norepinephrine release by **alpha-conotoxins** MII and AuIB microinjected into locus ceruleus)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 26 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:297438 HCAPLUS
DOCUMENT NUMBER: 130:297009
TITLE: Preparation and interaction of .alpha.-conotoxin peptides with neuronal nicotinic acetylcholine receptors
INVENTOR(S): Shon, Ki-joon; Olivera, Baldomero M.; Rivier, Jean E.; Koerber, Steven C.; Shen, Gregory S.; McIntosh, J. Michael; Cartier, G. Edward; Yoshikami, Doju
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA; Case Western Reserve University; Salk Institute; Cognetix, Inc.
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9921878 | A1 | 19990506 | WO 1998-US22368 | 19981023 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2308115 | AA | 19990506 | CA 1998-2308115 | 19981023 |
| AU 9911143 | A1 | 19990517 | AU 1999-11143 | 19981023 |
| EP 1032588 | A1 | 20000906 | EP 1998-953885 | 19981023 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001521042 | T2 | 20011106 | JP 2000-517986 | 19981023 |

PRIORITY APPLN. INFO.: US 1997-62783P P 19971024
US 1997-65814P P 19971114
WO 1998-US22368 W 19981023

OTHER SOURCE(S): MARPAT 130:297009

AB This invention relates to conopeptide MII derivs. Xaa-Cys-Cys-Xaa-Xaa1-Xaa2-Xaa-Cys-Xaa3-Xaa-Xaa4-Xaa5-Xaa-Xaa-Xaa-Cys (Xaa = natural, modified, of non-natural amino acid residue; modifications may be addn., substitution, or deletion of one or more amino acid residues; or include addn. or substitution of amino acid analogs; Xaa1 = any amino acid, preferably Asn or His; Xaa2 = any amino acid, preferably Pro or Hyp; Xaa3 = any amino acid, preferably His or Asn; Xaa4 = any amino acid, preferably Glu; Xaa5 = any amino acid, preferably His or Asn) in which amino acid residues are substituted as described herein while maintaining the basic activity of MII. The present invention also relates to the discovery of the 3-dimensional structure of MII, and the relationship of its structure to its specificity to the .alpha.3.beta.2 subtype of the neuronal nicotinic acetylcholine receptor (nAChR). The present invention also relates to computer based programs for the expression of the three-dimensional structure of MII and peptide analogs, peptide mimetics or non-peptide mimetics thereof. The structural characteristics may be correlated with biol. activity to enable the design of .alpha.-4/7 conotoxin peptide analogs and peptide mimetics which demonstrate the same specificity to neuronal nAChR. Such analogs and peptide mimetics are useful as cardiovascular agents and for treating or detecting small-cell lung carcinoma (SCLC).

IT **175735-93-0P, .alpha.-Conotoxin** MII
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and interaction of **.alpha.-conotoxin** peptides with neuronal nicotinic acetylcholine receptors)

IT **223416-40-8P 223416-43-1P, .alpha.-Conotoxin** Au IC **223416-44-2P 223416-45-3P**

**223416-46-4P 223416-48-6P 223416-49-7P**
**223416-50-0P 223416-51-1P 223416-52-2P**
**223416-53-3P 223416-54-4P 223416-55-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and interaction of **.alpha.-conotoxin** peptides with neuronal nicotinic acetylcholine receptors)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 27 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:275773 HCAPLUS
DOCUMENT NUMBER: 131:69359
TITLE: Identification of tyrosine sulfation in Conus pennaceus conotoxins .alpha.-PnIA and .alpha.-PnIB: further investigation of labile sulfo- and phosphopeptides by electrospray, matrix-assisted laser desorption/ionization (MALDI) and atmospheric pressure MALDI mass spectrometry
AUTHOR(S): Wolfender, Jean-Luc; Chu, Feixia; Ball, Haydn; Wolfender, Florence; Fainzilber, Michael; Baldwin, Michael A.; Burlingame, Alma L.
CORPORATE SOURCE: Department of Pharmaceutical Chemistry and Mass Spectrometry Facility, University of California, San Francisco, CA, 94143-0446, USA
SOURCE: Journal of Mass Spectrometry (1999), 34(4), 447-454
CODEN: JMSPFJ; ISSN: 1076-5174
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Liq. chromatog./electrospray ionization mass spectrometry was used to investigate the peptide compn. of the venom of Conus pennaceus, a molluscivorous cone shell from the Red Sea. Based on obsd. Mrs, this venom contained all known conotoxins previously isolated and identified from this species. Interestingly, the doubly protonated species of only two of these conotoxins, .alpha.-PnIA and .alpha.-PnIB, showed addnl. related ions at +40 m/z (+80 Da), indicating the presence of either sulfation or phosphorylation in both components. High-performance liq. chromatog. (HPLC) fractions contg. these two conotoxins were examd. by matrix-assisted laser desorption/ionization (MALDI) mass spectrometry in both pos. and neg. ion modes, as well as by MALDI high-energy collision-induced dissocn. These expts. established the presence of a single sulfated tyrosine residue within both .alpha.-PnIA and .alpha.-PnIB. Hence their post-translationally modified sequences are GCCSLPPCAANNPDY(S)C-NH2 (.alpha.-PnIA) and GCCSLPPCALSNPDY(S)C-NH2 (.alpha.-PnIB). This assignment was supported by comparison of their mass spectral behavior with that of known sulfated and phosphorylated peptides. This data clarified further the distinguishing features of the ionization and fragmentation of such modified peptides. Selective disulfide folding of synthetic .alpha.-PnIB demonstrated that both sulfated and non-sulfated toxins co-elute on reversed-phase HPLC and that .alpha.-PnIB possesses the

same disulfide connectivity as other "classical" .alpha.-conotoxins reported previously.

IT **157961-36-9, .alpha.-Conotoxin** Pn IA (reduced) **157998-82-8, .alpha.-Conotoxin** Pn IB (reduced)
RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)
(identification of tyrosine sulfation in Conus pennaceus conotoxins .alpha.-PnIA and .alpha.-PnIB and investigation of labile sulfo- and phosphopeptides by electrospray, MALDI, and atm. pressure MALDI mass spectrometry)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 28 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:168172 HCAPLUS
DOCUMENT NUMBER: 130:307784
TITLE: NMR Solution Structure of .alpha.-Conotoxin ImI and Comparison to Other Conotoxins Specific for Neuronal Nicotinic Acetylcholine Receptors
AUTHOR(S): Rogers, Jessica P.; Luginbuehl, Peter; Shen, Gregory S.; McCabe, R. Tyler; Stevens, Raymond C.; Wemmer, David E.
CORPORATE SOURCE: Department of Chemistry, University of California, Berkeley, CA, 94720, USA
SOURCE: Biochemistry (1999), 38(13), 3874-3882
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB .alpha.-Conotoxins, peptides produced by predatory species of Conus marine snails, are potent antagonists of nicotinic acetylcholine receptors (nAChRs), ligand-gated ion channels involved in synaptic transmission. We detd. the NMR soln. structure of the smallest known .alpha.-conotoxin, ImI, a 12 amino acid peptide that binds specifically to neuronal .alpha.7-contg. nAChRs in mammals. Calcn. of the structure was based on a total of 80 upper distance constraints and 31 dihedral angle constraints resulting in 20 representative conformers with an av. pairwise rmsd of 0.44 .ANG. from the mean structure for the backbone atoms N, C.alpha., and C' of residues 2-11. The structure of ImI is characterized by two compact loops, defined by two disulfide bridges, which form distinct subdomains sepd. by a deep cleft. Two short 310-helical regions in the first loop are followed by a C-terminal .beta.-turn in the second. The two disulfide bridges and Ala 9 form a rigid hydrophobic core, orienting the other amino acid side chains toward the surface. Comparison of the three-dimensional structure of ImI to those of the larger, 16 amino acid .alpha.-conotoxins PnIA, PnIB, MII, and EpI-also specific for neuronal nAChRs-reveals remarkable similarity in local backbone conformations and relative solvent-accessible surface areas. The core scaffold is conserved in all five conotoxins, whereas the residues in solvent-exposed positions are highly variable. The second helical region, and the specific amino acids that the helix exposes to solvent, may be particularly important for binding and selectivity. This comparative anal. provides a three-dimensional structural basis for

interpretation of mutagenesis data and structure-activity relationships for ImI as well other neuronal .alpha.-conotoxins.

IT **175735-93-0**, **.alpha.-Conotoxin** MII
**195823-99-5**, **.alpha.-Conotoxin** PnIB
**195824-00-1**, **.alpha.-Conotoxin** PnIA
**211050-66-7**, **.alpha.-Conotoxin** EpI
RL: PRP (Properties)
(NMR soln. structure of **.alpha.-conotoxin** ImI and comparison to other conotoxins specific for neuronal nicotinic acetylcholine receptors)

REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 29 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:764295 HCAPLUS
DOCUMENT NUMBER: 130:21651
TITLE: Toxic conopeptides AuIA, AuIB and AuIC of cone snail venom active against nicotinic receptors
INVENTOR(S): McIntosh, J. Michael; Cartier, G. Edward; Yoshikami, Doju; Luo, Siqin; Olivera, Baldomero M.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9851322 | A1 | 19981119 | WO 1998-US7004 | 19980409 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5866682 | A | 19990202 | US 1997-857068 | 19970515 |
| AU 9871043 | A1 | 19981208 | AU 1998-71043 | 19980409 |

PRIORITY APPLN. INFO.: US 1997-857068 19970515
WO 1998-US7004 19980409

OTHER SOURCE(S): MARPAT 130:21651

AB Peptides of 14-17 residues in length that are found in the venom of cone snails or analogs to the naturally available peptides, and which include two cyclizing disulfide linkages are described. These peptides are active against the .alpha.3.beta.4 subtype of the nicotinic acetylcholine receptor. More specifically, the present invention is directed to conopeptides having the general formula: Gly-Cys-Cys-Ser-Tyr-Xaa1-Xaa1-Cys-Phe-Ala-Thr-Asn-Xaa2-Xaa3-X aa4-Cys, wherein Xaa1 is Pro or Hyp (trans-4-hydroxy-Pro), Xaa2 is Ser, Pro or Hyp, Xaa3 is Gly or Asp and Xaa4 is a Tyr or des- Xaa4. The disulfide bridges are between the first and third between the second fourth cysteine residues. The C-terminal end is preferably

amidated. These peptides may be pharmaceutically useful.
IT **216299-20-6**, **.alpha.-Conotoxin** Au IA
**223416-43-1**, **.alpha.-Conotoxin** Au IC
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(toxic conopeptides AuIA, AuIB and AuIC of cone snail venom active against nicotinic receptors)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 30 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:676036 HCAPLUS
DOCUMENT NUMBER: 130:48561
TITLE: Three-Dimensional Solution Structure of .alpha.-Conotoxin MII by NMR Spectroscopy: Effects of Solution Environment on Helicity
AUTHOR(S): Hill, Justine M.; Oomen, Clasien J.; Miranda, Les P.; Bingham, Jon-Paul; Alewood, Paul F.; Craik, David J.
CORPORATE SOURCE: Centre for Drug Design and Development, The University of Queensland, Brisbane, 4072, Australia
SOURCE: Biochemistry (1998), 37(45), 15621-15630
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB .alpha.-Conotoxin MII, a 16-residue polypeptide from the venom of the piscivorous cone snail Conus magus, is a potent and highly specific blocker of mammalian neuronal nicotinic acetylcholine receptors composed of .alpha.3.beta.2 subunits. The role of this receptor type in the modulation of neurotransmitter release and its relevance to the problems of addiction and psychosis emphasize the importance of a structural understanding of the mode of interaction of MII with the .alpha.3.beta.2 interface. Here we describe the three-dimensional soln. structure of MII detd. using 2D 1H NMR spectroscopy. Structural restraints consisting of 376 interproton distances inferred from NOEs and 12 dihedral restraints derived from spin-spin coupling consts. were used as input for simulated annealing calcns. and energy minimization in the program X-PLOR. The final set of 20 structures is exceptionally well-defined with mean pairwise rms differences over the whole mol. of 0.07 .ANG. for the backbone atoms and 0.34 .ANG. for all heavy atoms. MII adopts a compact structure incorporating a central segment of .alpha.-helix and .beta.-turns at the N- and C-termini. The mol. is stabilized by two disulfide bonds, which provide cross-links between the N-terminus and both the middle and C-terminus of the structure. The susceptibility of the structure to conformational change was examd. using several different solvent conditions. While the global fold of MII remains the same, the structure is stabilized in a more hydrophobic environment provided by the addn. of acetonitrile or trifluoroethanol to the aq. soln. The distribution of amino acid side chains in MII creates distinct hydrophobic and polar patches on its surface that may be important for the specific interaction with the .alpha.3.beta.2 neuronal nAChR. A comparison of the structure

of MII with other neuronal-specific .alpha.-conotoxins provides insights into their mode of interaction with these receptors.

IT **175735-93-0, .alpha.-Conotoxin** MII
RL: PRP (Properties)
(three-dimensional soln. structure of **.alpha.-conotoxin** MII by NMR spectroscopy and effects of soln. environment on helicity)

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 31 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:475696 HCAPLUS
DOCUMENT NUMBER: 129:226831
TITLE: The 1.1 .ANG. Resolution Crystal Structure of [Tyr15]EpI, a Novel .alpha.-Conotoxin from Conus episcopatus, Solved by Direct Methods
AUTHOR(S): Hu, Shu-Hong; Loughnan, Marion; Miller, Russ; Weeks, Charles M.; Blessing, Robert H.; Alewood, Paul F.; Lewis, Richard J.; Martin, Jennifer L.
CORPORATE SOURCE: Centre for Drug Design and Development, University of Queensland, Brisbane, 4072, Australia
SOURCE: Biochemistry (1998), 37(33), 11425-11433
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Conotoxins are valuable probes of receptors and ion channels because of their small size and highly selective activity. .alpha.-Conotoxin EpI, a 16-residue peptide from the mollusk-hunting Conus episcopatus, has the amino acid sequence GCCSDPRCNMNNPDY(SO3H)C-NH2 and appears to be an extremely potent and selective inhibitor of the .alpha.3.beta.2 and .alpha.3.beta.4 neuronal subtypes of the nicotinic acetylcholine receptor (nAChR). The desulfated form of EpI ([Tyr15]EpI) has a potency and selectivity for the nAChR receptor similar to those of EpI. Here we describe the crystal structure of [Tyr15]EpI solved at a resoln. of 1.1 .ANG. using SnB. The asym. unit has a total of 284 non-hydrogen atoms, making this one of the largest structures solved de novo by direct methods. The [Tyr15]EpI structure brings to six the no. of .alpha.-conotoxin structures that have been detd. to date. Four of these, [Tyr15]EpI, PnIA, PnIB, and MII, have an .alpha.4/7 cysteine framework and are selective for the neuronal subtype of the nAChR. The structure of [Tyr15]EpI has the same backbone fold as the other .alpha.4/7-conotoxin structures, supporting the notion that this conotoxin cysteine framework and spacing give rise to a conserved fold. The surface charge distribution of [Tyr15]EpI is similar to that of PnIA and PnIB but is likely to be different from that of MII, suggesting that [Tyr15]EpI and MII may have different binding modes for the same receptor subtype.

IT **212758-79-7**
RL: PRP (Properties)
(1.1 .ANG. resoln. crystal structure of [Tyr15]EpI, a novel **.alpha.-conotoxin** from Conus episcopatus, solved by direct methods)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE

IN THE RE FORMAT

L12 ANSWER 32 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:400592 HCAPLUS
DOCUMENT NUMBER: 129:157855
TITLE: .alpha.-Conotoxin EpI, a novel sulfated peptide from Conus episcopatus that selectively targets neuronal nicotinic acetylcholine receptors
AUTHOR(S): Loughnan, Marion; Bond, Trudy; Atkins, Anne; Cuevas, Javier; Adams, David J.; Broxton, Natalie M.; Livett, Bruce G.; Down, John G.; Jones, Alun; Alewood, Paul F.; Lewis, Richard J.
CORPORATE SOURCE: Centre for Drug Design and Development, The University of Queensland, St. Lucia, 4067, Australia
SOURCE: Journal of Biological Chemistry (1998), 273(25), 15667-15674
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have isolated and characterized .alpha.-conotoxin EpI, a novel sulfated peptide from the venom of the molluscivorous snail, Conus episcopatus. The peptide was classified as an .alpha.-conotoxin based on sequence, disulfide connectivity, and pharmacol. target. EpI has homol. to sequences of previously described .alpha.-conotoxins, particularly PnIA, PnIB, and ImI. However, EpI differs from previously reported conotoxins in that it has a sulfotyrosine residue, identified by amino acid anal. and mass spectrometry. Native EpI was shown to coelute with synthetic EpI. The peptide sequence is consistent with most, but not all, recognized criteria for predicting tyrosine sulfation sites in proteins and peptides. The activities of synthetic EpI and its unsulfated analog [Tyr15]EpI were similar. Both peptides caused competitive inhibition of nicotine action on bovine adrenal chromaffin cells (neuronal nicotinic ACh receptors) but had no effect on the rat phrenic nerve-diaphragm (muscle nicotinic ACh receptors). Both EpI and [Tyr15]EpI partly inhibited acetylcholine-evoked currents in isolated parasympathetic neurons of rat intracardiac ganglia. These results indicate that EpI and [Tyr15]EpI selectively inhibit .alpha.3.beta.2 and .alpha.3.beta.4 nicotinic acetylcholine receptors.

IT **211050-66-7P, .alpha.-Conotoxin** Ep I
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**.alpha.-conotoxin** EpI is novel sulfated peptide from Conus episcopatus that selectively targets neuronal nicotinic acetylcholine receptors)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 33 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:394229 HCAPLUS
DOCUMENT NUMBER: 129:37452

TITLE: Use of .alpha.-conotoxin MII? to treat disorders resulting from nicotine-stimulated dopamine release

INVENTOR(S): McIntosh, J. Michael; Kulak, Jennifer M.; Yoshikami, Doju; Olivera, Baldomero M.

PATENT ASSIGNEE(S): University of Utah Research Foundation, USA

SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9824462 | A1 | 19980611 | WO 1997-US22350 | 19971205 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5780433 | A | 19980714 | US 1996-761674 | 19961206 |
| AU 9856909 | A1 | 19980629 | AU 1998-56909 | 19971205 |
| US 5922679 | A | 19990713 | US 1998-45925 | 19980323 |
| US 5929034 | A | 19990727 | US 1998-45926 | 19980323 |

PRIORITY APPLN. INFO.: US 1996-761674 19961206
WO 1997-US22350 19971205

AB Neuronal nicotinic acetylcholine receptors (nAChRs) are believed to mediate nicotine addiction. In addn., stimulation of nAChRs modulates release of neurotransmitters including dopamine, norepinephrine and serotonin. Thus, pharmacol. manipulation of nicotinic receptors has implications for a wide variety of disorders including psychotic, mood, movement and cognitive. For most nAChRs, there are no subtype selective ligands. However, .alpha.-conotoxin MII, a small peptide from the carnivorous marine snail Conus magus, was recently isolated. This peptide has been shown o be a specific antagonist for .alpha.3.beta.2 nicotinic receptors. The peptide potently blocks part, but not all, of nicotine-stimulated dopamine release from rat brain striatal synaptosomes. In contrast it has no effect on potassium stimulated dopamine release. Other .alpha.-conotoxins specifically target distinct neuronal nAChR subtypes. .alpha.-Conotoxins thus represent new lead compds. for CNS disorders.

IT **175735-93-0, .alpha.-Conotoxin** MII
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(use of **.alpha.-conotoxin** MII to treat disorders resulting from nicotine-stimulated dopamine release)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 34 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:351777 HCAPLUS

DOCUMENT NUMBER: 129:12744
TITLE: Use of conotoxin peptides ImI and MII as cardiovascular agents
INVENTOR(S): McIntosh, J. Michael; Olivera, Baldomero M.; Yoshikami, Doju
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA; McIntosh, J. Michael; Olivera, Baldomero M.; Yoshikami, Doju
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9822126 | A1 | 19980528 | WO 1997-US20669 | 19971117 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9852555 | A1 | 19980610 | AU 1998-52555 | 19971117 |
| AU 735724 | B2 | 20010712 | | |
| EP 948346 | A1 | 19991013 | EP 1997-947488 | 19971117 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001505878 | T2 | 20010508 | JP 1998-523732 | 19971117 |

PRIORITY APPLN. INFO.: US 1996-31141P P 19961118
WO 1997-US20669 W 19971117

AB ImI and MII conotoxin peptides, and derivs. thereof, are used as cardiovascular agents including, but not limited to, heart rate-regulating agents, blood pressure-regulating agents and antiarrhythmic agents.

IT **175735-93-0, .alpha.-Conotoxin** M II
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conotoxin peptides ImI and MII as cardiovascular agents)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 35 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:128874 HCAPLUS
DOCUMENT NUMBER: 128:240575
TITLE: Differential inhibition by .alpha.-conotoxin-MII of the nicotinic stimulation of [3H] dopamine release from rat striatal synaptosomes and slices
AUTHOR(S): Kaiser, S. A.; Soliakov, L.; Harvey, S. C.; Luetje, C. W.; Wonnacott, S.
CORPORATE SOURCE: Department of Biology and Biochemistry,

University of Bath, Bath, BA2 7AY, UK
SOURCE: Journal of Neurochemistry (1998), 70(3), 1069-1076
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The presynaptic nicotinic modulation of dopamine release from striatal nerve terminals is well established, but the subtype(s) of neuronal nicotinic acetylcholine receptor (nAChR) underlying this response has not been identified. Recently, .alpha.-conotoxin-MII has been reported to inhibit potently and selectively the rat .alpha.3.beta.2 combination of nAChR subunits. Here we have synthesized the peptide, confirmed its specificity, and examd. its effect on the (.+-.)-anatoxin-a-evoked release of [3H]-dopamine from rat striatal synaptosomes and slices. .alpha.-Conotoxin-MII (112 nM) completely blocked acetylcholine-evoked currents of .alpha.3.beta.2 nAChRs expressed in Xenopus oocytes (IC50 = 8.0.+-.1.1 nM). Pairwise combinations of other nicotinic subunits were not blocked by 112 nM .alpha.-conotoxin-MII. On perfused striatal synaptosomes and slices, .alpha.-conotoxin-MII dose-dependently inhibited [3H]dopamine release evoked by 1 .mu.M (.+-.)-anatoxin-a with IC50 values of 24.3.+-.2.9 and 17.3.+-.0.1 nM, resp. The dose-response curve was shifted to the right with increasing agonist concns. However, the maximal inhibition of responses achieved by .alpha.-conotoxin-MII (112 nM) was 44.9.+-.5.4% for synaptosomes and 25.0.+-.4.1% for slices, compared with an inhibition by 10 .mu.M mecamylamine of 77.9.+-.3.7 and 88.0.+-.2.1%, resp. These results suggest the presence of presynaptic .alpha.3.beta.2-like nAChRs on striatal dopaminergic terminals, but the incomplete block of (.+-.)-anatoxin-a-evoked [3H]dopamine release by .alpha.-conotoxin-MII also supports the participation of nAChRs composed of other subunits. The lower inhibition found in slices is consistent with an addnl. indirect nicotinic stimulation of dopamine release via an .alpha.-conotoxin-MII-insensitive nAChR.

IT **175735-93-0, .alpha.-Conotoxin-MII**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**.alpha.-conotoxin-MII** effect on dopamine release from striatal synaptosomes and slices in relation to nicotinic receptors)

L12 ANSWER 36 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:6399 HCAPLUS
DOCUMENT NUMBER: 128:19563
TITLE: Three-Dimensional Solution Structure of .alpha.-Conotoxin MII, an .alpha.3.beta.2 Neuronal Nicotinic Acetylcholine Receptor-Targeted Ligand
AUTHOR(S): Shon, Ki-Joon; Koerber, Steven C.; Rivier, Jean E.; Olivera, Baldomero M.; McIntosh, J. Michael
CORPORATE SOURCE: Department of Physiology and Biophysics, Case Western Reserve University, Cleveland, OH, 44106, USA
SOURCE: Biochemistry (1997), 36(50), 15693-15700
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The three-dimensional structure of .alpha.-conotoxin MII in aq. soln. has been detd. by two-dimensional 1H NMR spectroscopy. NOE-derived distances, refined by an iterative relaxation matrix approach, as well as dihedral and chirality restraints were used in high-temp. biphasic simulated annealing calcns. Fourteen min. energy structures out of 50 subjected to the SA simulations were chosen for evaluation; these 14 structures have a final RMS deviation of 0.76.+-.0.31 and 1.35.+-.0.34 .ANG. for the backbone and heavy atoms, resp. The overall structure is unusually well-defined due to a large helical component around the two disulfide bridges. The principal backbone folding motif may be common to a subclass of .alpha.-conotoxins. There are two distinct surfaces on the mol. almost at right angles to one another. One entirely consists of the hydrophobic residues Gly1, Cys2, Cys3, Leu15, and Cys16. The second comprises the hydrophilic residues Glu11, His12, Ser13, and Asn14. These surfaces on the ligand could be essential for the subtype-specific recognition of the receptor.
IT **175735-93-0, .alpha.-Conotoxin** MII
RL: PRP (Properties)
(three-dimensional soln. structure of **.alpha.-conotoxin** MII)

L12 ANSWER 37 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:577191 HCAPLUS
DOCUMENT NUMBER: 127:244160
TITLE: Crystal Structure at 1.1 .ANG. Resolution of .alpha.-Conotoxin PnIB: Comparison with .alpha.-Conotoxins PnIA and GI
AUTHOR(S): Hu, Shu-Hong; Gehrmann, John; Alewood, Paul F.; Craik, David J.; Martin, Jennifer L.
CORPORATE SOURCE: Centre for Drug Design and Development, University of Queensland, Brisbane, 4072, Australia
SOURCE: Biochemistry (1997), 36(38), 11323-11330
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Here, we describe the crystal structure of PnIB, solved at a resoln. of 1.1 .ANG. and phased using the Shake-and-Bake direct methods program. PnIB crystals are orthorhombic and belong to the space group P212121 with the following unit cell dimensions: a = 14.6 .ANG., b = 26.1 .ANG., and c = 29.2 .ANG.. The final refined structure of .alpha.-conotoxin PnIB includes all 16 residues plus 23 solvent mols. and has an overall R-factor of 14.7% (R-free of 15.9%). The crystal structures of the .alpha.-conotoxins PnIB and PnIA are solved from different crystal forms, with different solvent contents. Comparison of the structures reveals them to be very similar, showing that the unique backbone and disulfide architecture is not strongly influenced by crystal lattice constraints or solvent interactions. This finding supports the notion that this structural scaffold is a rigid support for the presentation of important functional groups. The structures of PnIB and PnIA differ in their shape and surface charge distribution from that of GI.
IT **195823-99-5, .alpha.-Conotoxin** Pn IB
**195824-00-1, .alpha.-Conotoxin** Pn IA

RL: PRP (Properties)
(crystal structure at 1.1 .ANG. resoln. of **.alpha.-conotoxin** PnIB in relation to **.alpha.-conotoxins** PnIA and GI)

L12 ANSWER 38 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:212436 HCAPLUS
DOCUMENT NUMBER: 126:208398
TITLE: Differential block of nicotinic synapses on B versus C neurons in sympathetic ganglia of frog by .alpha.-conotoxins MII and ImI
AUTHOR(S): Tavazoie, Sohail F.; Tavazoie, Masoud F.; Mcintosh, J. Michael; Olivera, Baldomero M.; Yoshikami, Doju
CORPORATE SOURCE: Department of Biology, University of Utah, Salt Lake City, UT, 84112, USA
SOURCE: British Journal of Pharmacology (1997), 120(6), 995-1000
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of two new acetylcholine receptor antagonists, .alpha.-conotoxin MII and .alpha.-conotoxin ImI, on nicotinic synaptic transmission in the 10th paravertebral sympathetic ganglion of the leopard frog (Rana pipiens) were examd. The preganglionic nerve was elec. stimulated (at low frequency, .ltoreq. min-1, to avoid use-dependent changes) while compd. action potentials of B and C neurons were monitored from the postganglionic nerve. .alpha.-Conotoxins MII and ImI, at low micromolar concns., reversibly blocked both B and C waves. .alpha.-Conotoxin MII blocked the C wave more effectively than the B wave, whereas the potency of .alpha.-conotoxin ImI was opposite that of MII. The observation that nicotinic antagonists can differentially block synaptic transmission of B vs. C neurons with opposite selectivities strongly suggests that these neurons possess distinct nicotinic receptors. In addn. to fast and slow B waves described by others, C waves with two temporally distinguishable components were present in our recordings. Each .alpha.-conotoxin affected fast and slow B waves similarly. Likewise, toxins did not discriminate between the two components of C waves. This suggests that all neurons within each major class (B or C) may have the same nicotinic receptors. Synthetic forms of .alpha.-conotoxins MII and ImI were used in the present study. Their ease of synthesis and their specificities should make these toxins useful probes to investigate the various subtypes of neuronal nicotinic acetylcholine receptors.

IT **175735-93-0, .alpha.-Conotoxin** MII
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(differential block of nicotinic synapses on B vs. C neurons in sympathetic ganglia by **.alpha.-conotoxins** MII and ImI)

L12 ANSWER 39 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:131527 HCAPLUS
DOCUMENT NUMBER: 126:234634
TITLE: Determinants of specificity for .alpha.-conotoxin MII on .alpha.3.beta.2

neuronal nicotinic receptors

AUTHOR(S): Harvey, Scott C.; Mcintosh, J. Michael; Cartier, G. Edward; Maddox, Floyd N.; Luetje, Charles W.

CORPORATE SOURCE: Department of Molecular and Cellular Pharmacology, University of Miami School of Medicine, Miami, FL, 33101, USA

SOURCE: Molecular Pharmacology (1997), 51(2), 336-342
CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The competitive antagonist .alpha.-conotoxin-MII (.alpha.-CTx-MII) is highly selective for the .alpha.3.beta.2 neuronal nicotinic receptor. Other receptor subunit combinations (.alpha.2.beta.2, .alpha.4.beta.2, .alpha.3.beta.4) are >200-fold less sensitive to blockade by this toxin. Using chimeric and mutant subunits, we identified amino acid residues of .alpha.3 and .beta.2 that participate in detn. of .alpha.-CTx-MII sensitivity. Chimeric .alpha. subunits, constructed from the .alpha.3 and .alpha.4 subunits, as well as from the .alpha.3 and .alpha.2 subunits, were expressed in combination with the .beta.2 subunit in Xenopus laevis oocytes. Chimeric .beta. subunits, formed from the .beta.2 and .beta.4 subunits, were expressed in combination with .alpha.3. Determinants of .alpha.-CTx-MII sensitivity on .alpha.3 were found to be within sequence segments 121-181 and 181-195. The 181-195 segment accounted for approx. half the difference in toxin sensitivity between receptors formed by .alpha.2 and .alpha.3. When this sequence of .alpha.2 was replaced with the corresponding .alpha.3 sequence, the resulting chimera formed receptors only 26-fold less sensitive to .alpha.-CTx-MII than .alpha.3.beta.2. Site-directed mutagenesis within segment 181-195 demonstrated that Lys 185 and Ile188 are crit. in detn. of sensitivity to toxin blockade. Determinants of .alpha.-CTx-MII sensitivity on .beta.2 were mapped to sequence segments 1-54, 54-63, and 63-80. Site-directed mutagenesis within segment 54-63 of .beta.2 demonstrated that Thr59 is important in detg. .alpha.-CTx-MII sensitivity.

IT **175735-93-0, .alpha.-Conotoxin** MII
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(determinants of specificity for **.alpha.-conotoxin** MII on .alpha.3.beta.2 neuronal nicotinic receptors)

L12 ANSWER 40 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:124468 HCAPLUS
DOCUMENT NUMBER: 126:126900

TITLE: Use of conotoxin peptides U002 and MII for treating or detecting small-cell lung carcinoma

INVENTOR(S): Olivera, Baldomera M.; Cruz, Lourdes J.; Hillyard, David R.; Mcintosh, J. Michael; Santos, Ameurfino S.

PATENT ASSIGNEE(S): University of Utah Research Fondation, USA

SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9640211 | A1 | 19961219 | WO 1996-US7962 | 19960604 |
| W: AU, CA, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5595972 | A | 19970121 | US 1995-487174 | 19950607 |
| AU 9662503 | A1 | 19961230 | AU 1996-62503 | 19960604 |
| AU 695055 | B2 | 19980806 | | |
| EP 844883 | A1 | 19980603 | EP 1996-921234 | 19960604 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 11506737 | T2 | 19990615 | JP 1996-500831 | 19960604 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1995-487174 | A | 19950607 |
| US 1993-84848 | A2 | 19930629 |
| US 1993-137800 | A2 | 19931019 |
| WO 1996-US7962 | W | 19960604 |

AB The present invention is directed to use of relatively short peptides, specifically the .alpha.-conotoxin peptides MII and UOO2, for treating patients with small-cell lung carcinoma (SCLC) or for detecting the presence of SCLC tumors. It has been discovered that while MII and UOO2 bind to neuronal nicotinic receptors as do other .alpha.-conotoxin peptides, they have a significantly lower affinity for neuromuscular receptors. Patients having SCLC are treated in accordance with the present invention by administering, preferably i.v. or i.m., a pharmaceutical compn. contg. the .alpha.-conotoxin peptide as the active ingredient. The presence or location of SCLC tumors are detected in accordance with the present invention by injecting a subject with MII or UOO2 labeled with a marker capable of detection and subsequently detecting the binding of the labeled MII or UOO2 to det. the presence or location of SCLC tumors.

IT **186420-62-2**, **.alpha.-Conotoxin** M II (reduced)
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(**.alpha.-conotoxin** peptides UOO2 and MII for treating or detecting small-cell lung carcinoma)

L12 ANSWER 41 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:85606 HCAPLUS
DOCUMENT NUMBER: 126:152786
TITLE: Conotoxin peptides
INVENTOR(S): Olivera, Baldomero M.; Cruz, Lourdes J.; Hillyard, David R.; Mcintosh, J. Michael; Santos, Ameurfino D.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: U.S., 35 pp., Cont.-in-part of U.S. 5,514,774.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| US 5595972 | A | 19970121 | US 1995-487174 | 19950607 |
| US 5432155 | A | 19950711 | US 1993-84848 | 19930629 |
| US 5514774 | A | 19960507 | US 1993-137800 | 19931019 |
| CA 2223737 | AA | 19961219 | CA 1996-2223737 | 19960604 |
| WO 9640211 | A1 | 19961219 | WO 1996-US7962 | 19960604 |
| W: AU, CA, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9662503 | A1 | 19961230 | AU 1996-62503 | 19960604 |
| AU 695055 | B2 | 19980806 | | |
| EP 844883 | A1 | 19980603 | EP 1996-921234 | 19960604 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 11506737 | T2 | 19990615 | JP 1996-500831 | 19960604 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1993-84848 | A2 | 19930629 |
| US 1993-137800 | A2 | 19931019 |
| US 1995-487174 | A | 19950607 |
| WO 1996-US7962 | W | 19960604 |

AB The invention is directed to A-lineage conotoxin peptides, which are conotoxin peptides that have strong homol. in the signal sequence and the 3'-untranslated region of the genes coding for these peptides to the sequences in the .alpha.-conotoxin peptides. The A-lineage conotoxin peptides include the .alpha.-conotoxin peptides, the .alpha.-conotoxin-like peptides and the .kappa.-conotoxin peptides, described further below. The .alpha.-conotoxin-peptides generally share a "core" sequence motif. This core sequence is termed the .alpha.3/5 core and is represented as Cys-Cys-Xaa-Xaa-Xaa-Cys-Xaa-Xaa-Xaa-Xaa-Xaa-Cys (SEQ ID NO: 1). The .alpha.-conotoxin-like peptides generally share a core sequence termed the .alpha.4/7 core and is represented as Cys-Cys-Xaa-Xaa-Xaa-Xaa-Cys-Xaa-Xaa-Xaa-Xaa-Xaa-Xaa-Xaa-Cys (SEQ ID NO:2). The .kappa.-conotoxin peptides generally have a core sequence termed the .kappa.7/2/1/3 core and is represented as Cys-Cys-Xaa-Xaa-Xaa-Xaa-Xaa-Xaa-Xaa-Cys-Xaa-Xaa-Cys-Xaa-Cys-Xaa-Xaa-Xaa-Cys (SEQ ID NO:3); .alpha.-conotoxins MII (SEQ ID NO:54) and U002 (SEQ ID NO:10) preferentially bind to neuronal nicotinic acetylcholine receptors, rather than neuromuscular receptors. These latter two conotoxins can be used to diagnose and treat small-cell lung carcinomas, which have cholinergic nicotinic receptors.

IT **186420-62-2, .alpha.-Conotoxin** M II (reduced)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**.alpha.-conotoxin** peptides for use as antitumor agents)

L12 ANSWER 42 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:34715 HCAPLUS
DOCUMENT NUMBER: 126:182612
TITLE: Identification of genes encoding A-lineage conotoxin peptides by PCR
INVENTOR(S): Olivera, Baldomero M.; Cruz, Lourdes J.; Hillyard, David R.; Mcintosh, J. Michael; Santos, Ameurfino D.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: U.S., 36 pp., Cont.-in-part of U.S. 5,514,774.

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5589340 | A | 19961231 | US 1995-477383 | 19950607 |
| US 5432155 | A | 19950711 | US 1993-84848 | 19930629 |
| US 5514774 | A | 19960507 | US 1993-137800 | 19931019 |

PRIORITY APPLN. INFO.: US 1993-84848 A2 19930629
US 1993-137800 A2 19931019

AB PCR primers for the identification of genes for A-lineage conotoxins are described. A-lineage conotoxin genes are very similar in the signal sequence and the 3'-untranslated region to the genes for .alpha.-conotoxins. The A-lineage conotoxins include the .alpha.-conotoxins, the .alpha.-conotoxin-like peptides and .kappa.-conotoxins. The .alpha.-conotoxin-peptides generally share a "core" sequence motif that is defined by the distribution of cysteines in the minimal biol. active peptide. A no. of novel conotoxins and conotoxin-like peptides are identified. These novel conotoxins may be of therapeutic or investigative use, for example, against tumor cells presenting cholinergic receptors such as small cell lung cancer cells.

IT **186420-62-2, .alpha.-Conotoxin** M II (reduced)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(amino acid sequence; process and primers for identifying nucleic acids encoding A-lineage conotoxin peptides)

L12 ANSWER 43 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:286546 HCAPLUS
DOCUMENT NUMBER: 124:335314
TITLE: The 1.1 .ANG. crystal structure of the neuronal acetylcholine receptor antagonist, .alpha.-conotoxin PnIA from Conus pennaceus
AUTHOR(S): Hu, Shu-Hong; Gehrmann, John; Guddat, Luke W.; Alewood, Paul F.; Craik, David J.; Martin, Jennifer L.
CORPORATE SOURCE: Center Drug Design and Development, Univ. Queensland, St. Lucia, 4072, Australia
SOURCE: Structure (London) (1996), 4(4), 417-423
CODEN: STRUE6; ISSN: 0969-2126
PUBLISHER: Current Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The 1.1 .ANG. crystal structure of synthetic PnIA was detd. by direct methods using the Shake-and-Bake program. The three-dimensional structure incorporates a .beta. turn followed by two .alpha.-helical turns. The conformation is stabilized by two disulfide bridges that form the interior of the mol., with all other side chains oriented outwards. The compact architecture of the PnIA toxin provides a rigid framework for presentation of chem. groups that are required for activity. The structure is characterized by distinct hydrophobic and polar surfaces; a 16 .ANG. sepn. of the

sole pos. and neg. charges (these two charged residues being located at opposite ends of the mol.); a hydrophobic region and a protruding tyrosine side chain. These features may be important for the specific interaction of PnIA with neuronal nAChR.

IT **157961-36-9, .alpha.-Conotoxin** Pn IA (reduced)
RL: PRP (Properties)
(crystal structure of conotoxin PnIA in relation to conformation)

L12 ANSWER 44 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:198722 HCAPLUS
DOCUMENT NUMBER: 124:281632
TITLE: A new .alpha.-conotoxin which targets .alpha.3.beta.2 nicotinic acetylcholine receptors
AUTHOR(S): Cartier, G. Edward; Yoshikami, Doju; Gray, William R.; Luo, Siqin; Olivera, Baldomero M.; McIntosh, J. Michael
CORPORATE SOURCE: Dep. Biology, Univ. Utah, Salt Lake City, UT, 84112, USA
SOURCE: Journal of Biological Chemistry (1996), 271(13), 7522-8
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have isolated a 16-amino acid peptide from the venom of the marine snail Conus magus which potently blocks nicotinic acetylcholine receptors (nAChRs) composed of .alpha.3.beta.2 subunits. This peptide, named .alpha.-conotoxin MII, was identified by electrophysiol. screening venom fractions against cloned nicotinic receptors expressed in Xenopus oocytes.the peptide's structure, which has been confirmed by mass spectrometry and total chem. synthesis, differs significantly from those of all previously isolated .alpha.-conotoxins. Disulfide bridging, however, is conserved. The toxin blocks the response to acetylcholine in oocytes expressing .alpha.3.beta.2 nAChRs with an IC50 of 0.5 nM and is 2-4 orders of magnitude less potent on other nAChR subunit combinations. We have recently reported the isolation and characterization of .alpha.-conotoxin ImI, which selectively targets homomeric .alpha.7 neuronal nAChRs. Yet other .alpha.-conotoxins selectively block the muscle subtype of nAChR. Thus, it is increasingly apparent that .alpha.-conotoxins represent a significant resource for ligands with which to probe structure-function relationships of various nAChR subtypes.

IT **175735-93-0P, .alpha.-Conotoxin** M II
RL: ADV (Adverse effect, including toxicity); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(new **.alpha.-conotoxin** and targeting of .alpha.3.beta.2 nicotinic acetylcholine receptors)

L12 ANSWER 45 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:601190 HCAPLUS
DOCUMENT NUMBER: 121:201190
TITLE: New Mollusk-Specific .alpha.-Conotoxins Block Aplysia Neuronal Acetylcholine Receptors

AUTHOR(S): Fainzilber, Michael; Hasson, Arik; Oren, Ruth; Burlingame, Alma L.; Gordon, Dalia; Spira, Micha E.; Zlotkin, Eliahu

CORPORATE SOURCE: Silberman Institute of Life Sciences, Hebrew University of Jerusalem, Jerusalem, 91904, Israel

SOURCE: Biochemistry (1994), 33(32), 9523-9
CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two mollusk-specific neurotoxic peptides from the venom of the molluscivorous snail Conus pennaceus are described. These new toxins block acetylcholine receptors (AChR) of cultured Aplysia neurons. Bath application of 0.5-1 .mu.M toxin induces 5-10-mV membrane depolarization, which recovers to the control level within 1-3 min in the presence of the toxin. This response is blocked by 1 mM hexamethonium. Concomitantly with the transient depolarization, the toxins block approx. 90% of the depolarizing responses evoked by brief iontophoretic application of acetylcholine. The pharmacol. and amino acid sequences of the toxins (.alpha.PnIA, GCCSLPPCAANNPDYC-NH2; .alpha.PnIB, GCCSLPPCALSNPDYC-NH2) enable their classification as novel .alpha.-conotoxins. The sequences differ from those of previously described.alpha.-conotoxins in a no. of features, the most striking of which is the presence of a single neg. charged residue in the C-terminal loop. This loop contains a pos. charged residue in piscivorous venom .alpha.-conotoxins. In contrast to other .alpha.-conotoxins, which are selective for vertebrate skeletal muscle nicotinic ACh receptors, these Conus pennaceus toxins block neuronal ACh receptors in molluscs. As such they are new probes which can be used to define subtypes of ACh receptors, and they should be useful tools in the study of structure-function relationships in ACh receptors.

IT **157961-36-9, .alpha.-Conotoxin** PnIA
**157998-82-8, .alpha.-Conotoxin** PnIB
RL: BIOL (Biological study)
(from Conus pennaceus, Aplysia neuronal acetylcholine receptor blockage by)

E1 THROUGH E65 ASSIGNED

FILE 'REGISTRY' ENTERED AT 11:33:27 ON 10 JAN 2003

L13 65 SEA FILE=REGISTRY ABB=ON PLU=ON (175735-93-0/BI OR 195823-99-5/BI OR 195824-00-1/BI OR 186420-62-2/BI OR 157961-36-9/BI OR 221639-83-4/BI OR 223416-43-1/BI OR 229639-63-8/BI OR 157998-82-8/BI OR 211050-66-7/BI OR 216299-20-6/BI OR 229639-64-9/BI OR 229639-65-0/BI OR 212758-79-7/BI OR 223416-40-8/BI OR 223416-44-2/BI OR 223416-45-3/BI OR 223416-46-4/BI OR 223416-48-6/BI OR 223416-49-7/BI OR 223416-50-0/BI OR 223416-51-1/BI OR 223416-52-2/BI OR 223416-53-3/BI OR 223416-54-4/BI OR 223416-55-5/BI OR 229639-60-5/BI OR 229639-61-6/BI OR 229639-62-7/BI OR 263028-53-1/BI OR 263028-54-2/BI OR 263028-55-3/BI OR 263028-56-4/BI OR 263028-57-5/BI OR 263028-58-6/BI OR 263028-59-7/BI OR 263028-61-1/BI OR 263028-62-2/BI OR 263028-63-3/BI OR 263028-64-4/BI OR 263028-65-5/BI OR 263028-66-6/BI OR 263028-67-7/BI OR 263028-68-8/BI OR 263028-69-9/BI OR 263028-70-2/BI OR 263028-71-3/BI OR 263028-72-4/BI OR 263028-73-5/BI OR

263028-74-6/BI OR 263028-75-7/BI OR 263028-76-8/BI OR
263028-77-9/BI OR 263028-78-0/BI OR 263028-79-1/BI OR
263028-80-4/BI OR 263028-81-5/BI OR 263028-82-6/BI OR
263028-83-7/BI OR 263028-84-8/BI OR 285558-22-7/BI OR
285558-23-8/BI OR 285558-24-9/BI OR 467428-30-4/BI OR
467428-33-7/BI)

L14 65 L13 AND L1

L14 ANSWER 1 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **467428-33-7** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-histidyl-L-prolyl-L-alanyl-L-cysteinyl-L-tyrosyl-L-alanyl-L-asparaginyl-L-asparaginyl-L-glutaminyl-L-.alpha.-aspartyl-L-tyrosyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 9: PN: WO02079236 SEQID: 9 claimed protein
SQL 16

SEQ 1 GCCSHPACYA NNQDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 137:289027

L14 ANSWER 2 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **467428-30-4** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-.alpha.-aspartyl-L-prolyl-L-arginyl-L-cysteinyl-L-asparaginyl-L-tyrosyl-L-.alpha.-aspartyl-L-histidyl-L-prolyl-L-.alpha.-glutamyl-L-isoleucyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2: PN: WO02079236 SEQID: 2 claimed protein
SQL 16

SEQ 1 GCCSDPRCNY DHPEIC
========= ======
HITS AT: 2-16

REFERENCE 1: 137:289027

L14 ANSWER 3 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **285558-24-9** REGISTRY
CN L-Cysteine, L-cysteinyl-L-cysteinyl-L-seryl-L-tyrosyl-L-prolyl-L-prolyl-L-cysteinyl-L-asparaginyl-L-valyl-L-seryl-L-tyrosyl-L-prolyl-L-.alpha.-glutamyl-L-isoleucyl- (9CI) (CA INDEX NAME)
SQL 15

SEQ 1 CCSYPPCNVS YPEIC
========== =====
HITS AT: 1-15

REFERENCE 1: 133:131093

L14 ANSWER 4 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **285558-23-8** REGISTRY
CN L-Cysteine, glycylglycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-tyrosyl-L-prolyl-L-prolyl-L-cysteinyl-L-asparaginyl-L-valyl-L-seryl-L-tyrosyl-

L-prolyl-L-.alpha.-glutamyl-L-isoleucyl- (9CI) (CA INDEX NAME)
SQL 17

SEQ 1 GGCCSYPPCN VSYPEIC
========= =======
HITS AT: 3-17

REFERENCE 1: 133:131093

L14 ANSWER 5 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **285558-22-7** REGISTRY
CN L-Cysteine, L-arginyl-L-alanyl-L-cysteinyl-L-cysteinyl-L-seryl-L-tyrosyl-L-prolyl-L-prolyl-L-cysteinyl-L-asparaginyl-L-valyl-L-asparaginyl-L-tyrosyl-L-prolyl-L-.alpha.-glutamyl-L-isoleucyl- (9CI) (CA INDEX NAME)
SQL 17

SEQ 1 RACCSYPPCN VNYPEIC
========= =======
HITS AT: 3-17

REFERENCE 1: 133:131093

L14 ANSWER 6 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-84-8** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-seryl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-asparaginyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSSPPCAL NNPDYC
========== ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 7 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-83-7** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-valyl-L-asparaginyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAV NNPDYC
========== ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 8 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-82-6** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-norleucyl-L-asparaginyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAX NNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 9 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-81-5** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-isoleucyl-L-asparaginyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAI NNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 10 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-80-4** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-methionyl-L-asparaginyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAM NNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 11 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-79-1** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-alanyl-L-alanyl-L-prolyl-L-prolyl-L-cysteinyl-L-leucyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCAAPPCLL SNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 12 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-78-0** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-alanyl-L-prolyl-L-prolyl-L-cysteinyl-L-leucyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSAPPCLL SNPDYC

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 13 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-77-9** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-alanyl-L-alanyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCAAPPCAL SNPDYC
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 14 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-76-8** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-threonyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPDTC
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 15 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-75-7** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-alanyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPDAC
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 16 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-74-6** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-alanyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPAYC
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 17 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-73-5** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-asparaginyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPNYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 18 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-72-4** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-3-hydroxy-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPDYC
========= ======
HITS AT: 2-16

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 132:246458

L14 ANSWER 19 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-71-3** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-.alpha.-aspartyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SDPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 20 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-70-2** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-glutaminyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SQPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 21 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-69-9** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-alanyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SAPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 22 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-68-8** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-alanyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL ANPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 23 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-67-7** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-leucyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL LNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 24 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-66-6** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-tryptophyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAW SNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 25 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-65-5** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-leucyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCLL SNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 26 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-64-4** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-seryl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCSL SNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 27 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-63-3** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinylglycyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCGL SNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 28 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-62-2** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-(4R)-4-hydroxy-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPXCAL SNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 29 OF 65 REGISTRY COPYRIGHT 2003 ACS

RN **263028-61-1** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-3-hydroxy-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPDYC
========= ======
HITS AT: 2-16

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 132:246458

L14 ANSWER 30 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-59-7** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-3-hydroxy-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPDYC
========= ======
HITS AT: 2-16

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 132:246458

L14 ANSWER 31 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-58-6** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-seryl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSSPPCAL SNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 32 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-57-5** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-alanyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSAPPCAL SNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 33 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-56-4** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-leucyl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCLLPPCAL SNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 34 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-55-3** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-alanyl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCALPPCAL SNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 35 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-54-2** REGISTRY
CN L-Cysteinamide, L-glutaminyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 QCCSLPPCAL SNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 36 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **263028-53-1** REGISTRY
CN L-Cysteinamide, N-acetylglycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPDYC
========= ======
HITS AT: 2-16

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 132:246458

L14 ANSWER 37 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **229639-65-0** REGISTRY
CN L-Cysteinamide, 3,5-diiodo-L-tyrosylglycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-asparaginyl-L-prolyl-L-valyl-L-cysteinyl-L-histidyl-L-leucyl-L-.alpha.-glutamyl-L-histidyl-L-seryl-L-asparaginyl-L-leucyl- (9CI) (CA INDEX NAME)
SQL 17

SEQ 1 YGCCSNPVCH LEHSNLC
========= =======
HITS AT: 3-17

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 131:82983

L14 ANSWER 38 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **229639-64-9** REGISTRY
CN L-Cysteinamide, 3-iodo-L-tyrosylglycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-asparaginyl-L-prolyl-L-valyl-L-cysteinyl-L-histidyl-L-leucyl-L-.alpha.-glutamyl-L-histidyl-L-seryl-L-asparaginyl-L-leucyl- (9CI) (CA INDEX NAME)
SQL 17

SEQ 1 YGCCSNPVCH LEHSNLC
========= =======
HITS AT: 3-17

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 131:82983

L14 ANSWER 39 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **229639-63-8** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-alanyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAA SNPDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 132:246458

REFERENCE 2: 132:132466

REFERENCE 3: 131:82983

L14 ANSWER 40 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **229639-62-7** REGISTRY
CN L-Cysteinamide, L-tyrosylglycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-tyrosyl-L-prolyl-L-prolyl-L-cysteinyl-L-phenylalanyl-L-alanyl-L-threonyl-L-asparaginyl-L-seryl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (3.fwdarw.9),(4.fwdarw.17)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 17

SEQ 1 YGCCSYPPCF ATNSDYC
========= =======
HITS AT: 3-17

REFERENCE 1: 131:82983

L14 ANSWER 41 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **229639-61-6** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-asparaginyl-L-prolyl-L-valyl-L-cysteinyl-L-phenylalanyl-L-alanyl-L-threonyl-L-histidyl-L-seryl-L-asparaginyl-L-leucyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCFA THSNLC
========= ======
HITS AT: 2-16

REFERENCE 1: 131:82983

L14 ANSWER 42 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **229639-60-5** REGISTRY
CN L-Cysteinamide, L-tyrosylglycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-asparaginyl-L-prolyl-L-valyl-L-cysteinyl-L-histidyl-L-leucyl-L-.alpha.-glutamyl-L-histidyl-L-seryl-L-asparaginyl-L-leucyl-, cyclic (3.fwdarw.9),(4.fwdarw.17)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 17

SEQ 1 YGCCSNPVCH LEHSNLC
========= =======
HITS AT: 3-17

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 131:82983

L14 ANSWER 43 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **223416-55-5** REGISTRY
CN .alpha.-Conotoxin M II, 15-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCHL EHSNAC
========= ======
HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 44 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **223416-54-4** REGISTRY
CN .alpha.-Conotoxin M II, 14-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCHL EHSALC
========= ======
HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 45 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **223416-53-3** REGISTRY
CN .alpha.-Conotoxin M II, 13-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCHL EHANLC
========= ======
HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 46 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **223416-52-2** REGISTRY
CN .alpha.-Conotoxin M II, 12-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCHL EASNLC
========= ======
HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 47 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **223416-51-1** REGISTRY
CN .alpha.-Conotoxin M II, 11-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCHL AHSNLC
========= ======
HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 48 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **223416-50-0** REGISTRY
CN .alpha.-Conotoxin M II, 10-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCHA EHSNLC
========= ======
HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 49 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **223416-49-7** REGISTRY
CN .alpha.-Conotoxin M II, 9-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCAL EHSNLC
========= ======
HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 50 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **223416-48-6** REGISTRY

CN .alpha.-Conotoxin M II, 7-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPACHL EHSNLC
========= ======
HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 51 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **223416-46-4** REGISTRY
CN .alpha.-Conotoxin M II, 5-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSAPVCHL EHSNLC
========= ======
HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 52 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **223416-45-3** REGISTRY
CN .alpha.-Conotoxin M II, 4-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCANPVCHL EHSNLC
========= ======
HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 53 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **223416-44-2** REGISTRY
CN .alpha.-Conotoxin M II, 1-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 ACCSNPVCHL EHSNLC
========= ======
HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 54 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **223416-43-1** REGISTRY
CN .alpha.-Conotoxin Au IC (9CI) (CA INDEX NAME)
OTHER NAMES:
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-tyrosyl-L-prolyl-L-prolyl-L-cysteinyl-L-phenylalanyl-L-alanyl-L-threonyl-L-asparaginyl-L-serylglycyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide)
SQL 16

SEQ 1 GCCSYPPCFA TNSGYC
========= ======
HITS AT: 2-16

REFERENCE 1: 131:82983

REFERENCE 2: 130:297009

REFERENCE 3: 130:21651

L14 ANSWER 55 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **223416-40-8** REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-asparaginyl-L-prolyl-L-valyl-L-cysteinyl-L-phenylalanyl-L-alanyl-L-threonyl-L-asparaginyl-L-seryl-L-leucyl-L-asparaginyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCFA TNSLNC
========= ======
HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 56 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **221639-83-4** REGISTRY
CN .alpha.-Conotoxin Pn IA, 10-L-leucine-15-desulfo- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL NNPDYC
========== ======
HITS AT: 1-16

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 132:246458

REFERENCE 2: 132:132466

REFERENCE 3: 131:82983

REFERENCE 4: 130:267767

L14 ANSWER 57 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **216299-20-6** REGISTRY
CN .alpha.-Conotoxin Au IA (9CI) (CA INDEX NAME)
OTHER NAMES:
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-tyrosyl-L-prolyl-L-prolyl-L-cysteinyl-L-phenylalanyl-L-alanyl-L-threonyl-L-asparaginyl-L-seryl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide)
SQL 16

SEQ 1 GCCSYPPCFA TNSDYC
========= ======
HITS AT: 2-16

REFERENCE 1: 131:82983

REFERENCE 2: 130:21651

L14 ANSWER 58 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **212758-79-7** REGISTRY

CN .alpha.-Conotoxin Ep I, 15-desulfo- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSDPRCNM NNPDYC
========= ======
HITS AT: 2-16

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 129:226831

L14 ANSWER 59 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **211050-66-7** REGISTRY
CN .alpha.-Conotoxin Ep I (9CI) (CA INDEX NAME)
OTHER NAMES:
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-.alpha.-aspartyl-L-prolyl-L-arginyl-L-cysteinyl-L-asparaginyl-L-methionyl-L-asparaginyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-O-sulfo-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide)
SQL 16

SEQ 1 GCCSDPRCNM NNPDYC
========= ======
HITS AT: 2-16

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 130:307784

REFERENCE 2: 129:157855

L14 ANSWER 60 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **195824-00-1** REGISTRY
CN .alpha.-Conotoxin Pn IA (9CI) (CA INDEX NAME)
OTHER NAMES:
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-alanyl-L-asparaginyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-O-sulfo-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide)
SQL 16

SEQ 1 GCCSLPPCAA NNPDYC
========= ======
HITS AT: 2-16

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 132:318808

REFERENCE 2: 132:246458

REFERENCE 3: 132:237373

REFERENCE 4: 132:132466

REFERENCE 5: 132:9825

REFERENCE 6: 131:82983

REFERENCE 7: 130:307784

REFERENCE 8: 127:244160

L14 ANSWER 61 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **195823-99-5** REGISTRY
CN .alpha.-Conotoxin Pn IB (9CI) (CA INDEX NAME)
OTHER NAMES:
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-O-sulfo-L-tyrosyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide)
SQL 16

SEQ 1 GCCSLPPCAL SNPDYC
========= ======
HITS AT: 2-16

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 132:318808

REFERENCE 2: 132:246458

REFERENCE 3: 132:237373

REFERENCE 4: 132:132466

REFERENCE 5: 132:9825

REFERENCE 6: 131:82983

REFERENCE 7: 130:307784

REFERENCE 8: 127:244160

L14 ANSWER 62 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **186420-62-2** REGISTRY
CN .alpha.-Conotoxin M II (reduced) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCHL EHSNLC
========= ======
HITS AT: 2-16

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 126:182612

REFERENCE 2: 126:152786

REFERENCE 3: 126:126900

L14 ANSWER 63 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **175735-93-0** REGISTRY
CN .alpha.-Conotoxin M II (9CI) (CA INDEX NAME)
OTHER NAMES:

CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-asparaginyl-L-prolyl-L-valyl-L-cysteinyl-L-histidyl-L-leucyl-L-.alpha.-glutamyl-L-histidyl-L-seryl-L-asparaginyl-L-leucyl-, cyclic (2.fwdarw.8),(3.fwdarw.16)-bis(disulfide)
SQL 16

SEQ 1 GCCSNPVCHL EHSNLC
========= ======
HITS AT: 2-16

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 138:540

REFERENCE 2: 137:273401

REFERENCE 3: 137:226853

REFERENCE 4: 137:76110

REFERENCE 5: 137:59609

REFERENCE 6: 136:396263

REFERENCE 7: 136:273496

REFERENCE 8: 136:65411

REFERENCE 9: 135:271222

REFERENCE 10: 135:137700

L14 ANSWER 64 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **157998-82-8** REGISTRY
CN .alpha.-Conotoxin Pn IB (reduced) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-O-sulfo-L-tyrosyl-
SQL 16

SEQ 1 GCCSLPPCAL SNPDYC
========= ======
HITS AT: 2-16

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 131:69359

REFERENCE 2: 121:201190

L14 ANSWER 65 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN **157961-36-9** REGISTRY
CN .alpha.-Conotoxin Pn IA (reduced) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-alanyl-L-asparaginyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-O-sulfo-L-tyrosyl-

SQL 16

SEQ 1 GCCSLPPCAA NNPDYC
========= ======

HITS AT: 2-16

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE 1: 131:69359

REFERENCE 2: 124:335314

REFERENCE 3: 121:201190

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